THE NONVENEREAL DISEASES OF THE GENITALS

The Nonvenereal Diseases of the Genitals

Etiology Differential Diagnosis and Therapy

By

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PREFACE

During the first two decades of the Twentieth Century important discoveries in both venereal and nonvenereal diseases focused attention upon the management of diseases affecting the genital region.

The discovery of the treponema pallidum the Wassermann reaction and Ehrlich's Salvarsan in almost uninterrupted succession led the way to a greater understanding in the management of syphilis During the same time, modern virology was born. Cellular research revealed the significance of inclusion bodies, probably harboring the virus corpuscles. Lymphogranuloma venereum, hitherto known only as "climatic bubos" was recognized as the virus produced fourth venereal disease. The virus etiology of various diseases of the skin such as common warts, molluscum contagiosum and herpes simplex appeared evident. Their transmissibility from man to man was demonstrated. Progress in the cultivation of the gonococcus Neisseri enabled its distinction from pseudogonococci. Obscure conditions of the genital region, mistaken for tuberculosis or syphilis, were proven to be fungous in origin.

Soon after World War I the textbooks of dermatology and venereology had to be brought up to date to include these discoveries. Because of the nature of such texts, the differential diagnosis between venereal and nonvenereal diseases of the genitals was extended throughout the various chapters. A comprehensive discussion of these diagnostic problems in their entirety did not exist.

In 1924 an attempt was made to describe the most important nonvenereal diseases of the genitals and to discuss their diagnostic importance in a concise form, useful for the general practitioner The demand for a second edition in 1928 and translations of this book into Italian and Spanish seemed to further indicate the need for such a book.

Twenty-five years have passed. New revolutionary discoveries have again pushed forward the boundaries of knowledge and with it the management of both venereal and nonvenereal diseases of the genital region. Progress in internal medicine has revealed the relation of certain genital diseases to dysfunction of the endocrine glands, to metabolic disturbances and to nutritional deficiencies. The introduction of the electron microscope

Callomon, Fritz T *Die Nichtvenerischen Genitalerkrankungen*. Leipzig, Georg Thieme, 1924 and 1928.

has led to discoveries in cellular research and to the demonstration of virus corpuscles thus corroborating the classification of molluscum contagiosum, condyloma acuminatum warts herpes lymphogranuloma venereum, vaccinia and others as virus diseases Chemotherapeutic research has revolutionized the treatment of syphilis and gonorrhea as well as of genital lesions from other causes The discovery of the sulfonamides and in recent times, of the antibiotics has opened a new era in the fight against venereal disease.

Re-evaluation in the light of present knowledge has produced changes in classification of many conditions. For instance the relationship of aphthous lesions to ectodermosis pluriorificialis Behcet s syndrome and erythema multiforme exudativum has been widely discussed. A close relationship between lichen sclerosus et atrophicans balanitis xerotica obliterans and kraurosis penis has been pointed out

In view of all of these factors, the authors of the present book realized that after two and one half decades an entirely new book would have to be written It is hoped that the present book *The Nonvenereal Diseases of the Genitals* Etiology Differential Diagnosis and Therapy will stimulate the practitioner to examine the well known symptoms of the venereal diseases from an opposite viewpoint. In this way he can recognize or at least be acutely conscious of the enormously multitudinous manifestations of those diseases of the anogenital region other than syphilis chancroid and gonorrhea.

We are grateful to American and foreign authors especially Drs O Gans (Frankfurt) M Monacelli (Naples) and M B Sulzberger (New York) for the use of valuable photographs to supplement our own

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INTRODUCTION

(*The Problem "VENEREAL versus "NONVENEREAL"*)

The term nonvenereal" has been used for practical purposes, to designate the large group of diseases involving the genital organs which are not dependent on sexual intercourse. This term serves to draw special attention to various affections of the genitals and has found widespread use in the world literature so that while there may be some objections to its use, there are these good reasons for its acceptance.

In the strictest sense the word nonvenereal" is not distinct enough to render sharp differentiation of this group of diseases from the common venereal diseases of the genitals, such as syphilis, chancroid, and gonorrhea. It is not unusual for syphilis to be transmitted in an extragenital manner In addition gonococcal conjunctivitis of the newborn is due to infection occurring during the passage of the infant through the infected birth canal. Also the gonorrheal vulvovaginitis in children is usually caused by indirect contamination of the bed sheets or towels soiled with pus

On the other hand, there are nonvenereal diseases which occasionally have been transmitted to the genitals from other regions of the body Balanitis erosiva circinata et gangrenosa, caused by fusospirochetosis, has occasionally been found to be transmitted from patients with Vincent s angina, produced by the same symbiotic micro-organisms. Herpes simplex may be transmitted by sexual intercourse, as well as by other means.

Thus, while we are well aware of the wide scope of the term nonvenereal, the frequent and practical use which it has served, justifies its continued usage.

For the proper diagnosis of a venereal disease, one must know which diseases are nonvenereal, and be able to recognize them. In all textbooks on venereology great attention has been paid to accurate descriptions of the appearance of venereal diseases however in many textbooks it may appear that too little attention has been paid to the multitude of diagnostic problems arising from the great variety of nonvenereal affections occa sionally occurring in the genital region

Infectious and non infectious processes manifestations of constitutional diseases as well as dermatoses, dermatomycoses and neoplasms are frequently located in the genital region and may even occur without

involvement of the other areas of the body Non-gonorrheal urethritis (nonspecific urethritis) and nonspecific diseases of the testis, epididymis and of the corpora cavernosa confront the physician with a multitude of diagnostic problems

This book therefore will be helpful in the differentiation between the manifestations of the common venereal diseases and the great variety of other conditions of the genitals

In addition attention had to be focused upon the etiology and pathogenesis of those affections which are not derived from venereal infection. The peculiar appearance of the dermatoses localized in the genital region, as well as certain rare conditions of the penis, scrotum and vulva demanded special consideration in our discussion.

The nonvenereal diseases of the lower urinary tract have been included in the description This description will not replace, but may to some extent, supplement the respective descriptions in textbooks dealing with diseases of the urogenital system The distinction of gonorrheal from non-gonorrheal (nonspecific) urethritis, orchitis and epididymitis has become one of the major problems in the venereological clinics and dispensaries

According to the modern achievements of research, it may seem that gonorrhea and possibly also syphilis will gradually lose their foremost significance in the differentiation of the various affections of the genitals. Owing to the frequently dramatic results obtainable by the administration of sulfonamides and antibiotics in patients with gonorrhea and syphilis, the proportion between venereal and nonvenereal affections may have changed in many centers of modern therapy

Increasing experience however has shown that too optimistic conclusions should be looked at with some reservation. In spite of the dramatic effectiveness of the new powerful drugs one should not overlook the fact that also the limits of their action have been recognized. An exaggerated optimism will easily result in slackening the surveillance of the patients after modern treatment. Moreover in spite of the great achievements of the Public Health Service in combating venereal disease a great number of infections still are and will remain undetected and untreated. There remains the intricate problem to get hold of all vectors of the infectious micro-organisms and in particular to bring under control hidden prostitution.

If there were extreme optimists who in view of modern therapeutic methods may predict, in a not too remote future, that venereal diseases would have lost much of their importance and that their incidence would be gradually outnumbered by nonvenereal affections of the genitals one should not forget the teachings of History of Medicine

As Rudolph Virchow the renowned pathologist of the Nineteenth Century said at another time of fundamental medical discoveries "Research has never yielded a complete knowledge. We are always on the way like travellers during a great journey None of us should ever expect to reach our definite goal. Time and again, the wide land of the Unknown will open, and whatever we may have discovered, we never will be entirely satisfied. Human knowledge is a flowing matter Only Faith and Confidence have the privilege to remain constant at any moment

This is the naturalist's way For as there exists a community of learned men, there also exists a common feeling of humility and a patient submission to the insurmountable limits of human knowledge.

Working itself is the scientist's reward. Beyond this source of satisfaction, the highest recompensation will be bestowed upon us when we succeed in conducing scientific progress toward actual life, not alone for materialistic purposes but also for the benefit of the ethical progress of mankind."

Quoted and translated from R. Virchow *Four Lectures on Life and Disease* (Berlin, George Reimer 1862) dedicated to the sister of the noted physiologist Johannes Muller

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THE NONVENEREAL DISEASES OF THE GENITALS

PART I

CHAPTER 1

PYOGENIC DISEASES OF THE ANOGENITAL REGION

Impetigo	Carbuncle
Pyoderma	Erysipelas
Ecthyma	Pyogenic Granuloma
Folliculitis	Hidradenitis Suppurativa
Furunculosis	References

During the last two decades there have been notable changes occurring in the incidence course and management of pyogenic diseases. The sulfonamides and later antibiotics account for many of these changes Some of these diseases such as erysipelas and carbuncle have almost disappeared in many hospitals of the United States while others have been somewhat altered. Improper use of certain of these therapeutic agents has produced added complications in general management of patients such as the tendency of these substances to produce allergic sensitization when applied topically In general, however both the sulfonamides and the antibiotics have improved the therapeutic approach to pyogenic infections.

Impetigo

This most superficial of the pyogenic diseases does not frequently involve the anogenital region, except in infants when the diaper area is involved because of rapid spread of the pyogenic infection under this closely covered moist covering The flaccid nature of the bulla, with rapid rupture, leaving either the fine covering of epidermis or the superficial denuded area, can then be seen. The more commonly seen, heavy piled-up crust is not found in this type of impetigo

In the adult, the same eruption may also appear but usually only as an accompaniment of the same infection occurring elsewhere and transferred to the anogenital region by the hands.

Bockhart's impetigo is a superficial pustular eruption not infrequently found in the anogenital region of infants.

A staphylococcal origin prevails in the etiology of impetigo In addition, however there exists a streptococcal type Mixed cases occur The clinical distinctiveness of either form has been subject to many discussions The reader is referred to F Lewandowsky's elaborate studies

(*Arch Dermat u Syph* 94 163 1909) and to the *Transactions of the Congress of the German Dermatological Society in Hamburg*, 1921 (*Arch. Dermat u Syph.*, *138*·438 1922)

Pyoderma

Pyoderma is a deeper pyogenic infection than impetigo It is usually staphylococcic in origin, but other organisms have been reported. As the name implies the appearance is suggestive of pus on the skin. With a tendency to crusting, the color of the crust varies according to the serous, seropurulent or bloody contents of the secretion. It may be yellow or green depending on the organism, or red to brown and black, according to the amount of blood.

Pyoderma is a common complication of the parasitic infestations of the skin and is often found in the anogenital region as part of a general picture of scabies.

Ecthyma

Ecthyma can involve the anogenital region, but is more frequently found on the extremities especially in the anterior tibial regions, but



FIGURE 1 Ecthyma in terminal lymphatic leukemia.

as the disease is auto-inoculable, it can appear in the anogenital region In this area the heavy piled up crust becomes softened, because of moisture and friction in this area, so that unlike the typical clinical appearance of the lesion with the usually heavy piled up crust, a different picture is presented with punched-out soft ulcers having a granulating, bleeding red base and a red, inflammatory aureola.

Folliculitis

Folliculitis is frequently seen in the anogenital region. The natural conditions of this area, with moisture and the presence of numerous hair

follicles, allows the ready entrance of pyogenic organisms to produce this disease. Typically one finds a superficial pustule pierced by a hair While oils and tars are at times causative agents, the general features of the



FIGURE 2. Folliculitis and secondary intertrigo of the genital region.

area alone are sufficient to permit ready access of the invading organisms. In hot weather and warmer climates this condition can be quite persistent.

Furunculosis

Deeper abscess formation in the region of the hair follicle may cause a furuncle. Here again, the moisture and lack of aeration of the anogenital area lends itself readily to such infections and a variable number of organisms may be at fault.

Carbuncle

As the invasive organisms spread through the tissues following furuncle formation the lesions can enlarge and so involve wide areas of tissue. Such spread is now readily combatted with the antibiotics. The abscess formation may then penetrate through the skin at widely spaced areas, discharging pus to the surface.

Erysipelas

Erysipelas is another of the severe and dangerous pyogenic infections which has been reduced in incidence with the arrival of newer forms of therapy However in countries where antibiotics were or still are not sufficiently available, erysipelas did not lose its practical importance and its serious character

Erysipelas of the genitals is usually accompanied by excessive edematous swelling of the prepuce scrotum or the labia majora The anatomical structure and in particular the abundant supply of these tissues with lymphatics explains the development of sometimes grotesque enlarge-



FIGURE 3 Erysipelas. Edema of the cutis and inflammatory infiltration. Loosening of epithelium from papillary bodies. (*Handb d. Haut u Geschlechtsk., IX* 1 33 Springer Berlin, 1929)



FIGURE 4. Erysipelas. Streptococci in tissue magnif. × 1640 (Delbanco) (*Handb d. Haut u Geschlechtsk., IX* 1 35. Springer Berlin, 1929)

ments, similar to the intense swelling in erysipelas of the lips eyelids or ear lobes

Recurrent erysipelas of the genital and inguinal regions may leave chronic edema and in the course of frequent subsequent attacks may result in productive lymphangitis with elephantiasic thickenings of the

scrotum or the labia majora. These complications are discussed in Chapter 16

Histology: The Figures 3 and 4 demonstrate (a) edema and inflammation of the involved tissue, and (b) the accumulation of streptococci in the tissue of the cutis.

Pyogenic Granuloma

Pyogenic granuloma is an unusual form of pyoderma. Predominantly located on the face, the fingers or palms of the hands, it may occur casually on the scrotum or vulva. Granuloma pyogenicum (Crocker) or telangiectatic granuloma has been described in the United States by Hartzell (1904)

Pyogenic granuloma develops usually in connection with staphylococcic infections (Wile) not infrequently in connection with a preceding traumatic lesion It appears either as a pedunculated or as a sessile granulation tumor (ten sessile lesions among twenty nine cases Michelson, 1925) Its pea to hazelnut-sized, smooth, pinkish to dark red proliferations may persist for an undetermined time. If the lesion is pedunculated, the thin pedunculus may be completely overlapped by the mushroom like tumor (case of Isbruch telangiectatic granuloma of the *labium majus*) Such a lesion exposed to injury will bleed easily fine brownish or greenish gray crusts may be left.

Histologically pyogenic granuloma presents a fan-like irregular vascularization and perivascular hypertrophy It is rich in endothelial epithelioid and plasma cells. Biopsy may be necessary to exclude a possible malignant transformation.

Hidroadenitis Suppurativa

Hidroadenitis suppurativa is a chronic recurring pyogenic infection of the apocrine glands of the skin While the most common location is in the axillae, this disease assumes most annoying features when it affects the anogenital area.

It manifests itself as tender red swollen nodules which are slow in eroding to the surface. Incision of these lesions usually reveals only a small amount of pus, which seems out of proportion to the actual symptomatology Staphylococci have usually been found in the pus from these lesions. Friction and traumatization may cause a most painful disorder in hidroadenitis suppurativa of the anogenital region.

After a number of months with frequent recurrences, scar tissue forms and tends to produce linear bands At times sinus tracts will form from repeated infection in such scar tissue. Comedones can be seen in the glandular orifices.



FIGURE 5. Hidroadenitis suppurativa, perianal region.



FIGURE 6. The same patient, note scars.



FIGURE 7. Hidroadenitis suppurativa, left axilla, the same patient.

Differential Diagnosis

Pyogenic disease of the anogenital region requires differentiation from a great variety of dermatoses. Impetigo in its vesicular pustular or crusted stages must be distinguished from herpetic lesions eczematous eruptions with vesicles, pustules and crusts, drug eruptions, acne, pemphigus and pustular or ulcerated syphilitic eruptions. The small vesicles and erosions due to herpes progenitalis are readily distinguished from impetigo by their circular or polycyclic borders and their grouped location in a limited area herpes progenitalis is a self healing condition.

Vesicular pustular or crusted eczematous eruptions cause larger in flammatory infiltrated, oozing or crusted patches of various size itching may be marked in this type. Impetigo superimposed upon oozing eruptions leads to the formation of heavy piled-up crusts in the affected areas.

Eruptions of pemphigus vulgaris are rarely limited to the anogenital area the characteristic development and spread of the bullae, the course and the general condition contrast markedly with vesicular impetiginous eruptions

After lifting the crust from a lesion of impetigo a superficial erosion remains, whereas the crust formed in ulcerating syphilitic lesions covers an indurated ulcer Circinate or annular forms of impetigo which are only occasionally found in the genital region demand distinction from super ficial tinea circinata or from gyrate superficial syphiloma.

Ecthyma of the genital region also needs to be differentiated from ulcerative syphiloma. The acute development, the inflammatory aspect and irregular shape of ecthymatous lesions however contrast with the chronic course, the gyrate or circular form, and the induration of such syphilitic lesions.

Small furuncles are readily distinguished from small papulo-pustular syphilomas which do not show the acute inflammation of furuncles and are in contrast with a developing furuncle, painless.

Pyogenic granuloma may require differentiation from small angiom atous tumors and occasionally from angiosarcoma.

Hidroadenitis suppurativa will be readily recognized in presence of the same condition in the axillae although in occasional instances other chronic diseases producing scarring and sinus tract formation such as lymphogranuloma venereum, may present a problem. A negative Frei test would tend to exclude the latter diagnosis.

Treatment

The use of an antibiotic ointment such as neomycin is of more prac- tical use in the routine treatment of pyogenic diseases of the skin than the

determination of sensitivity of the organisms to the various antibiotics. The latter study requires several days and is a relatively expensive procedure. However where any further question of expense arises it is well to remember that ointments containing 3 per cent ammoniated mercury are quite satisfactory for treatment of these affections in many cases.

It may occur that ointments are harmful in the routine treatment of these infections as grease folliculitis may develop in the anogenital region and so cause unfavorable complications and even spread of the condition In such instances it is often helpful to make use of a less greasy lotion such as neomycin lotion as described by Forbes for daytime application, reserving the use of the antibiotic ointments for night time use.

The use of the antibiotics has revolutionized the management of hidroadenitis suppurativa and whereas formerly it was common to see such infections carry on for periods of years it seems that now early treatment can check its progress in most instances

In these cases it seems advisable to study the isolated organism for antibiotic sensitivity and then be prepared to carry out the treatment with the appropriate antibiotic over a period of several months.

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CHAPTER 2

DERMATOMYCOSES OF THE ANOGENITAL REGION

( ) Superficial
- Introduction
- Tinea Cruris (Eczema Marginatum)
- Erythrasma
- Tinea Versicolor
- F vus
- Moniliasis

(b) Deep
- Blastomycosis
- Coccidioidomycosis
- Actinomycosis
- Sporotrichosis and Related Fungous Infections
- References

(a) Superficial Dermatomycoses

Introduction

The anogenital region is a site of predilection for various dermatomycoses In spite of many similarities in their clinical course and manifestations, these affections are caused by a great variety of fungi. Modern mycology has considerably enlarged our knowledge of the morphology biology cultivation and classification of these organisms. But additional information is still needed.

Some of the causal fungi belong to the ectothrix type, growing in the epidermal layers but only outside of the hair shafts. Others such as the trichophyton species or the achorion Schoenleini, belong to the ecto-endothrix type that also invades the hairs.

Many of these organisms have been found as saprophytes on the skin of healthy persons. They thrive readily on the softened skin in intertriginous regions. Heat, sweat and constant contact of opposing surfaces of the skin will contribute to transform these fungi into virulent pathogenic agents. A circumscribed superficial lesion may develop and persist as a chronic mycosis for years without any change and frequently unnoticed by the patient. Even itching may be absent.

However under the influence of a superimposed acute intertrigo such dormant mycoses will rapidly activate. Thus a banal intertriginous dermatitis may camouflage a spreading dermatomycosis of the inguinal folds subsequently involving the genitals. The onset of violent itching will suggest the mixed nature of such a condition.

To a large extent, the biological properties of the causative fungi are the major determinants of the type of cutaneous manifestation as well as

of the course of the infectious process However it is not only the topical preparedness of the exposed skin that is of essential importance, but also the general predisposition of the subject.

Research has shown that in accordance with the individual power of defense, immunization processes may be elicited in association with the local tissue reaction to mycotic infection Some slight degree of local immunity may persist for a limited time beyond the healing period. Anemia, malnutrition and internal disease, in particular diabetes may impair the power of cell defense The control of these conditions is important to prevent recurrences.

Characteristic of all superficial mycoses caused by the propagation of saprophytic fungi is (1) the propagation of the mycotic organisms in the uppermost layers of the skin provoking an inconspicuous tissue reaction (2) the abundant presence of mycotic elements responsible for the affection, and the tendency to recur after a temporary disappearance (3) the existence of an individual predisposition to such infection, and (4) the exceedingly low degree of infectiousness in resistant individuals (Plaut)

Tinea Cruris (Eczema Marginatum)

In 1860 Hebra described eczema marginatum as a particular form of eczema, characterized by (1) its constant location on the internal surfaces of the upper parts of the thighs, pubic and gluteal regions (2) its tendency to peripheral expansion and central regression and (3) its sharply demarcated, slightly elevated margin where the eczematous process is more pronounced. During the following decade the transmissibility of this affection was proved by Koebner (1864)

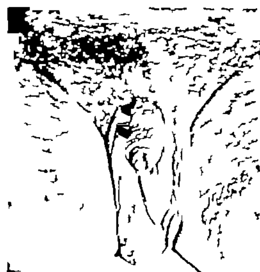


FIGURE 8. Tinea cruris.

Clinical symptoms: Hebra's clinical description is still valid. The inguinal and anogenital areas are predominantly affected Occasionally this mycotic infection is located in the axillary and submammary areas, and occasionally between the toes (Sabouraud, 1912) However primary lesions are uncommon in regions other than the inguinal folds and the anogenital area. Violent itching accompanies the cutaneous reaction.

The initial lesion of tinea cruris appears as a reddish patch with marginal papules and vesicles The latter leave minute, brownish crusts distributed over the growing patch. Circular lesions may coalesce with adjacent patches into larger polycyclic lesions. Small satellite lesions are frequently found around an older plaque

Spreading very slowly the lesions may extend to the lower abdomen up to the umbilicus or may involve the anal region and the gluteal skin. The penis and scrotum usually remain intact. Continuous scratching produces lichenification and a darker central pigmentation of the mycotic area. In other cases, there are large scaling erythematous plaques with configurated outlines

Sabouraud, in his study on an epidemic of eczema marginatum in a boarding school, distinguished three clinical types (1) Hebra's type



FIGURE 9 Epidermophyton inguinale drawing made from Sabouraud. (*Arch. f Dermat u Syph.*, *113* 923, Fig 5)

marginée (2) a "type erythémateux non-marginèe" and (3) a type eczématoide.

Intense sweating or softening of the skin by wet compresses will stimulate the growth of the fungus. Exacerbations occur following long, strenuous military marches or long automobile rides, especially when intertrigo develops as a complication.

Transmissions from one person to another have been observed and could be traced to the common use of towels or blankets in dormitories or barracks We found no mention of conjugal transmission

Etiology: The definition of tinea cruris (eczema marginatum) as a specific dermatomycosis has been established since Sabouraud (1907) discovered the causative fungus, which he named *epidermophyton inguinale* (the *epidermophyton floccosum*" of the American nomenclature) The

fungus is easily demonstrable in scrapings from the borders of the lesion after adding a few drops of a 15 to 20 per cent solution of potassium hydroxide or a drop of Loeffler's methylene blue on the cover glass Cultures grow slowly on maltose agar especially on Sabouraud's medium.

This organism may also affect the feet with redness scaling and maceration similar to that produced by the Trichophyton gypseum

The *differential diagnosis* includes other superficial dermatomycoses, certain forms of seborrheic dermatitis, and occasionally circinate forms of psoriasis and syphiloma. The distinction from other fungous infections will depend upon identification by culture Textbooks of dermatology provide the necessary mycological information Clinically the papulovesicular margin and the tendency to increase in size are the decisive symptoms, suggesting eczema marginatum Circular psoriasis presents a coarser lamellar desquamation and a more reddish color Other psoriatic eruptions may be found on the well known sites of predilection Circinate and annular syphilomas have an indurated border and a more brownish appearance.

Therapy: Tinea cruris responds rapidly to fungicidal agents Several brushings with tincture of iodine may suffice to control circumscribed small patches Definitely effective are ointments containing undecylenic acid, salicylic acid (1 per cent) or sulfur (5 per cent) Also an ointment containing 0.5 to 1 per cent of chrysarobin in equal parts of lanolin and aquaphor has proved effective but must be used with caution.

Following disappearance of the lesions, an after treatment should follow consisting of salicylic acid (1 per cent) and resorcinol (5 per cent) in aqueous or alcoholic solution, painted on twice daily avoiding the scrotum. Recurrences, otherwise frequent, may be prevented by this procedure.

Erythrasma

Erythrasma is a chronic, superficial mycotic infection limited to the upper and middle layers of the stratum corneum. Without causing any inflammatory reaction and not even itching, this condition may escape the patient's attention for a long time. The inner surfaces of the thighs the groins and the anogenital region are the sites of erythrasma. Occasionally a location in the axillary folds has been found.

The initial lesion consists of a punctiform to pin head size spot. The lesions spread slowly forming larger patches up to the size of a palm. As a rule the eruption shows a symmetrical distribution. The lesions are at first slightly reddish but subsequently change to a yellowish red, red brown and often to dark brown. When thriving upon an area of intertriginous dermatitis the fungus proliferates very rapidly as indicated by the onset of intense itching The eczematous process may completely cover the concomitant mycosis

Erythrasma is transmissible. Conjugal infection has been reported in rare instances.

Etiology: The specific fungus of erythrasma was detected by Burchardt (1859) and was named "*microsporon minutissimum* by Baerensprung (1862) at present, this fungus is known as *nocardia minutissimum*." Masses of this delicate hyphomycete found in scrapings produce a picture very similar to that obtained in tinea versicolor Mycelia and conidia, however are smaller than in the latter condition. The densely septiferous mycelia frequently show a curved configuration the filaments encompass numerous round to square spores.



FIGURE 10. Erythrasma. Fungus identified by microscope (Callomon. Die Nichtvenerischen *Genitalerkrankungen* G Thieme, Leipzig, 1928)

Differential diagnosis: The differentiation of nocardia minutissimum from microsporon furfur the fungus of tinea versicolor is all the more difficult since these two organisms appear almost identical also in their cultural behavior In addition the microscopical recognition of nocardia minutissimum may prove difficult because of the likelihood of mistaking intraepithelial spaces in a scraping sample for the delicate hyphae of this fungus. Clinically the wide distribution of the multiple lesions in tinea versicolor is in distinct contrast to the characteristic location of erythrasma. Erythrasma differs from tinea cruris by the lack of marginal vesicles and in general an absence of inflammatory reaction.

Tinea Versicolor (Pityriasis Versicolor [Willan] or Chromophytosis)

In contradistinction to the predominant anogenital location of erythrasma, this area constitutes one, but by far not a common site for tinea versicolor In their initial stages tinea versicolor and erythrasma are morphologically almost identical. Fully developed erythrasma however presents a brownish red color markedly different from the yellowish (café-au-lait) color of the patches in tinea versicolor As to the size of the lesions, it must be considered that tinea versicolor may produce not

only the characteristic, round or discoid finely scaling yellowish lesions, but also larger patches with circular or polycyclic borders

As in erythrasma, pruritus is almost lacking in tinea versicolor Intense sweating causes reddening and a more distinct configuration of the tinea versicolor eruptions For the most part patients with perigenital tinea versicolor present typical eruptions also in more typical locations (the chest, particularly the sternal groove back, shoulders and axillae) In our patient pictured in Figure 11 tinea versicolor of the groins and genital region was associated with widespread eruptions on the chest and the shoulders



FIGURE 11 Tinea versicolor

Etiology: The fungus of tinea versicolor was described by Eichstaedt in 1846 under the name of *microsporon furfur*" (*malassezia furfur* of recent nomenclature) Its mycelia and spores are coarser than those of nocardia minutissimum

Histology: The microscopic features of both erythrasma and tinea versicolor present a massed accumulation of fungi in the corneal stratum of the epidermis, the middle layers being more involved than its upper layers. The propagating fungi loosen the structure of this stratum inter spersing the texture of the stratum corneum with a dense network of mycelia and spores. Inflammatory symptoms or changes of the prickle cells and basal cells are incidental and are usually due to secondary infection or eczematization.

Differential diagnosis: In white patients the appearance of a disseminated eruption of tinea versicolor may resemble a mottled hyperpigmentation of the skin. In colored people the mycotic patches often appear as distinct spots lighter than the surrounding skin.

In contradistinction to erythrasma and tinea versicolor the pigmentary changes due to *vitiligo* of the inguinal and genital regions show no scaling, not even after scratching as in tinea versicolor The demonstration of fungi is always essential in differential diagnosis.

Syphilitic macular exanthemas may involve the lower abdomen, the groins and thighs as a rule, they are distributed over the entire trunk, the upper arms, thighs hands and neck. Their livid red color contrasts with the yellowish color of tinea versicolor Incidentally a syphilitic roseola may appear in association with a previously existing eruption of the mycosis. In the clinical differentiation of tinea versicolor golden yellow to dark brown fluorescence under Wood's light is of definite aid.

Therapy: Erythrasma and tinea versicolor respond to the same treatment as that described for tinea cruris In many cases daily baths, combined with rubbing the affected skin areas with strong soap, will suffice to control these mycoses. Care should be taken, however with this method, that further irritation is not produced. After rinsing and drying, the additional application of an ointment containing salicylic acid (1 per cent) and sulfur (5 per cent) twice daily is recommended. After-treatment should consist of repeated daily application of an aqueous or alcoholic solution of salicylic acid (1 per cent)

Tinea Circinata

Tinea circinata occurs occasionally as an isolated mycotic infection of the anogenital region. Superficial, and occasionally deep fungous infections of this type have been observed especially in the inguinocrural and perianal regions. Mycology classification and cultural behaviour are discussed in dermatological textbooks and monographs

Superficial tinea circinata occurring in those regions produces circular or polycyclic lesions with vesicular and scaling margins, such as is seen elsewhere on the skin.

Tinea circinata may be complicated by superimposed *intertriginous* inflammation and may thus extend over the perianal and scrotal skin. Occasionally the infiltrative form of *deep* fungous infection tinea profunda, has been observed on the hairy portions of the anogenital skin in patients with tinea profunda of the bearded region.

Differential diagnosis: Tinea circinata must be differentiated from annular and circinate syphilomas, plaques of psoriasis, lesions caused by seborrheic dermatitis and occasionally pityriasis rosea. Superficial tinea

circinata is characterized by its fine vesicles and scaling marginal zone and presents usually a more reddish color than the darker pigmented syphiloma. Itching is usually constant in tinea circinata. Neither syphilomas nor psoriatic plaques cause itching. Spots of seborrheic dermatitis have a more yellowish color than superficial tinea circinata, showing a slight crust formation in association with the scaling process.

The demonstration of the fungus in scrapings and by culture is of paramount importance.

Occasionally an initial lesion of *pityriasis rosea* may be situated on the upper half of the thighs or the lower abdomen and thus be mistaken for tinea circinata. Such a "herald spot" often persists as a single lesion several centimeters in diameter for several weeks before the generalized eruption appears. The negative results of mycologic studies will then exclude fungous infection.

The etiology of pityriasis rosea is still unknown. No evidence of mycotic origin has been produced. Morphological similarities with mycotic infections alone do not justify the assumption of an unknown fungus. Moreover, the presence of a causative fungus would hardly escape modern mycological examination.

Therapy. Treatment of tinea circinata of the genital region is similar to that of superficial fungous infections elsewhere on the body: painting with tincture of iodine, ointments containing fungicidal compounds such as undecylenic acid as recommended in dermatological textbooks. Epilation is indicated in the rare cases of the deep infiltrative form of tinea profunda infection in the anogenital region. Roentgen epilation, however, is contraindicated in this location because of secondary sequellae.

Strong applications of salicylic acid (above 3 per cent) should be avoided because of local irritation. Asterol® [2-dimethylamine-6-(beta diethylamino-ethoxy) benzo-thiazole dihydrochloride] ointment should be avoided in the anogenital region, not only because of proximity to the mucous membranes but also because of the frequency of accompanying acute eczematous changes.

However, if secondary changes are also present, such as intertrigo, these should be treated first.

Favus

Favus infection of the genitals occurs either secondary to favus of the scalp by autoinoculation with the patient's scratching fingers, or as an isolated infection caused by various species of achorion, such as a. Schoenleini (favus capillitii) or achorion Quinckeanum (the fungus of favus of the mouse and cat).

Next to the scalp, the scrotum provides a site of predilection for favus infection. Dubreuilh's description of a case of *scrotal favus* frequently

cited in the earlier literature, is still the classical example, showing favus of both the hairy and non-hairy scrotal skin There were eighty five follicles involved with yellow scutulae at the sites of implantation of the hairs, with a coincident herpetiform patch with tiny vesicles on the contact surface of the neighboring thigh. Tomkinson reported favus of the *penis*, scrotum and the contact surfaces of the thighs. Isolated favus infection of the *vulva* is extremely rare and no mention of such cases is made in recent American literature.

As in favus of the scalp typical yellow scutula are also formed in scrotal favus However the characteristic appearance of this dermatomy cosis may be altered in scrotal favus by the presence of grayish or brownish crusts, and, on the non hairy skin, of marginated patches like tinea circinata.

Differential diagnosis: When scrotal favus is secondary to infection of the scalp or of other parts of the body the diagnosis suggests itself In *isolated* favus of the genitals, the presence of sulfur yellow scutulae will suggest possible favus infection. In less characteristic cases, with crust formation the dryness and friability of the crusts and the dusty aspect of the loosened hairs piercing these coverings are of diagnostic importance. A helpful aid in the diagnosis of favus scutulae is the A. Neisser test, i.e., swabbings with alcohol will reproduce the golden yellow color of the typical scutulum. Removal of the brittle crusts and the infected hairs may leave depressions at the site of implantation In chronic cases, the atrophic stage of the destroyed follicles will be recognizable in some areas

The differentiation of favus of the genitals from other conditions demands the demonstration of achorion in the scutula and infected hairs especially in patches resembling tinea circinata.

Therapy: Many of the measures found successful in the treatment of favus of the scalp have been found useful also for favus of the genital region However Roentgen epilation, a long established method of treat ment for favus capillitii, cannot be recommended for favus of the scrotum, because of the inherent danger of Roentgen damage to the testicles. No treatment whatsoever should be initiated before the involved surfaces have been thoroughly cleansed of scales and crusts. In all cases the hair should be removed with forceps. Treatment with fungicidal ointments, like those applied in other dermatomycoses must follow It may be necessary to change the ointments and solution repeatedly

Favus of the non hairy areas is rarely serious and repeated swabbing with a tincture of iodine solution may suffice to control superficial mycotic plaques.

Moniliasis

Occasional findings of yeast or yeast like organisms among the bacterial flora of the preputial sac or the vulva have been known for some

time. For a long time their presence was believed to be practically of no importance Not before World War I had evidence been produced, that yeast or yeast like organisms may cause skin lesions resembling those of intertrigo eczematous conditions or pyogenic affections.

Yeast mycoses develop chiefly in areas of the body exposed to friction, heat and moisture. The genital region ranks first among the sites of predilection.

The most common fungus acting as a pathogenic agent in yeast infections of the genitals is *candida (monilia) albicans* (the Oidium albicans of foreign authors) Occasionally related species have been demonstrated



FIGURE 12. Moniliasis (Callomon Die Nichtvenerischen *Genitalerkrankungen*. G Thieme, Leipzig, 1928)

as causal organisms (saccharomyces) The mycology classification and methods of cultivation of these fungi are described in textbooks of skin diseases.

Candida albicans occurs as a saprophyte on and around the finger nails and on normal skin, and is thus easily transmitted to other regions of the body (Jesmer and Kleiner) It has also been found in the oral cavity of healthy persons and in normal stools. It is frequently found in the stools of children with thrush (Benham Falchi, *et al.*) The same fungus is known as a most common saprophyte of the normal vagina and vulva. Campbell and Parrott (1950) found that about 15 per cent of the patients coming to a gynecological clinic harbor candida albicans about 38 per cent among these patients showing signs of a yeast vulvo-vaginitis.

The proof of the specificity of candida albicans in a given case is often

difficult because mycelia and spores of monilia are not infrequently found in association with bacteria in smears taken from acute dermatoses, balanitis etc. The question then arises whether the monilia and related organisms are purely incidental findings or play only a secondary role in a given case.

The evidence of *specificity* depends on (1) constant identical findings of mycelia and spores in smears (2) identification of monilia by culture, and (3) transmissibility to man and animal (Falchi) The potential pathogenicity of candida albicans has been proven both clinically and experimentally by many investigators. Falchi and other experimenters succeeded



FIGURE 13. Candida albicans in culture (*Ibidem*)

in producing analogous lesions in man and animals by inoculation of autogenous culture material, always with identical mycologic findings on the same media following each re-inoculation.

A most important factor is the individual *susceptibility* to such infection. It depends on (1) a local predisposition favored by hyperhidrosis, softening of the skin by wet compresses closed bandages or prolonged baths, and (2) a *general* predisposition favored by anemia, cachexia, internal disease, obesity and especially by *diabetes*.

Clinical features: Moniliasis occurs in the anogenital and inguinocrural areas, the axillary submammary or interdigital folds, around the finger nails, and in association with oral thrush in infants on the labial corners (perlèche) Moniliasis may occur as an isolated affection or in association with moniliasis of other areas of the body (perianal lesions in infants with oral thrush, submammary infections in mothers of suckling infants)

The *primary* lesion appears either as a vesicle the size of a pinhead that may develop into a pustule or as a lentil shaped, slightly elevated, discoid erythematous macule with a fine central lamellar scaling Increasing in number the denuded vesicles leave erosions which may coalesce to excoriations with a polycyclic border line Erythematous initial lesions may spread into larger scaling patches with a yellowish-white margin, consisting of a loosening brittle and friable epidermis Extension occurs by development and enlarging of new patches Trichophytosis like forms may develop

Circular eruptions of pustules especially in the inguinocrural folds, or miliaria like eruptions have been described by Staeheli (*dermatitis pustulosa oidiomycetica*) and by Miescher (*miliaria rubra oidiomycetica*)

When located in the genitocrural folds in combination with intertrigo, the fungous infection spreads readily to the surface of the scrotum or the labia majora, occasionally including the mons pubic. Perianal moniliasis readily spreads from the anal folds over the perineum An intense pruritus is common in monilial infections

Moniliasis of the genital region has been observed as a *conjugal infection* Falchi describes a case in a woman of fifty two years, showing large erythematous erosive and squamous lesions the husband presented a more acute desquamative dermatitis of the scrotum and the contact surfaces of the thighs. Benedek reported a case of monilial vaginitis in a wife with monilial balanitis in the husband contracted by marital intercourse. The primary infection of the wife could be traced to the repeated use of a monilia infested vaginal douche nozzle that had been wrapped in a wet cloth.

Monilial Vulvitis

Monilial vulvitis and *vaginitis* develop especially in the advanced stages of pregnancy or in diabetic women. The condition is frequently but not necessarily associated with cutaneous lesions. Vaginal monilial infection presents itself either as a diffuse superficial vaginitis of grayish white mycotic coverings. Giulini described isolated monilial vaginitis without involvement of the vulva the whole vaginal mucosa was affected including the cervix uteri

Monilial Balanitis and Balanoposthitis

As in vulvitis diabetica, so also in the analogous condition of the male, the softened epithelial layers of the preputial sac and the development of erosions render a most suitable medium for mycotic growth In addition the continual contact with the sugar containing urine acts as a growth stimulating factor In monilial vulvitis as well as in monilial balanitis, a

largely mixed flora of micro-organisms is seen in the majority of cases It may occur that the presence of hyphomycetes and spores is thoroughly overshadowed by the multitude of other organisms. In other cases, mycotic elements may dominate the microscopic picture.

Genital moniliasis in *sucklings* or *infants* is primarily located around the *anus* and is derived from monilia-containing stools in association with thrush. Anogenital moniliasis has also been reported independently of thrush as an isolated condition in male and female infants Mycelia and spores are demonstrable in the small vesicles or in squamous erythematous areas of this region

Brief reference to the rare *systemic* monilia infections should not be omitted. In their pulmonary and gastrointestinal forms the prognosis is serious. In some such cases, there may occur id like cutaneous eruptions disseminated over parts of the skin. It is often difficult to bring these secondary monilids under therapeutic control (Sulzberger and Wolf)

Differential diagnosis: The etiological diagnosis depends definitely upon the demonstration of the causal fungus particularly in cases camouflaged by a pre-existing intertrigo Identification by culture is likewise decisive for the distinction of moniliasis from trichophytosis and in vulvovaginitis oidomycotica, from diphtherial and pseudodiphtherial infections. Herpetic eruptions and erosions differ from monilasis by their grouping, their aspect, their limited extent and duration. For culture, particles of epidermal residue and the contents of pustules are required. The most commonly used media are dextrose or maltose-agar and in particular Sabouraud's medium.

Therapy: In every instance of monilial balanoposthitis and vulvovaginitis a careful inquiry must be made as to possible coincidental diabetes which must be controlled by insulin and/or dietary therapy in order to prevent relapses of the monilial infection.

Differentiation of generalized or systemic moniliasis can be made from acrodermatitis enteropathica, according to Dillaha, Lorincz and Aavik, because in the latter yeasts cannot invariably be demonstrated in skin lesions, the viscera lack usual monilial lesions there is an intermittent rather than a steady progressive course, there is total alopecia rather than partial defluvium associated with cachexia, and there is a distinct familial tendency

Cutaneous moniliasis responds promptly to local application of bactericidals and disinfectants in ointments or solutions Ointments containing resorcinol (2 to 3 per cent) and salicylic acid (1 per cent) may suffice to cure anogenital moniliasis in infants. The widely used and effective application of 1 to 2 per cent solutions of gentian violet, two or three times a day is recommended for monilial lesions in the inguinocrural region.

Dressings with solutions of mercuric chloride (1 2,000 to 5 000) are useful in vulvar moniliasis. In monilial vaginitis, irrigations with mercury chloride solutions of low concentraton (1 8 000 to 10 000) are widely used. In patients who are sensitive to mercuric compounds the mercury chloride solutions may be replaced by potassium permanganate solution (1 5 000)

(b) Deep Dermatomycoses

Blastomycosis

Cutaneous blastomycosis, although rarely observed as a localized affection in the anogenital region, must be included in the differential diagnosis of infectious lesions in this area.

Following Busse's and Buschke's first description of blastomycosis (1894) numerous fungous infections of different origin have been described under this designation. Cutaneous and systemic infections have been attributed to a great variety of yeasts yeast like organisms or budding fungi. Confusion soon arose as to the terminology and classification of such infections. Castellani (1930) pointed out that the term "*cutaneous blastomycosis*" indicates a clinical rather than a mycological entity or to be more correct, a group of closely allied entities characterized by the presence of granulomatous, papillomatous or framboesiform lesions in which certain yeast like fungi are found.

Two well-defined forms of blastomycosis have been distinguished, namely the *European blastomycosis* (type described by Busse and Buschke) and the *North American blastomycosis* or Gilchrist's disease (Gilchrist, 1896)

The *Busse Buschke type* of blastomycosis occurs as a deep infiltrative and a superficial form. Acneiform or pustular lesions appear at the site of a surface infection. These lesions eventually break down and are transformed into papillomatous or gummatous ulcers. The scant gray or brownish viscous secretion contains shreds of necrotic tissue and numerous yeast like organisms.

The superficial form has been described as interdigital blastomycosis (Kaufmann Wolf) or as "blastomycosis superficialis erosiva of the inguinal and genital region Fabry described this superficial form on the female genitals. In one case he demonstrated the causal fungus from an intertriginous dermatitis of the inguinal folds and of the adjacent parts of the vulva. In a second patient the entire vulva and the inguinal region showed the characteristic stages of erosion and epithelization in a net like pattern. Urinalysis in this case revealed diabetes, which came as a surprise to the patient.

The fungi described by Buschke were *ascomycetes* showing endog

enous sporulation or in other cases, yeast like organisms with no spore formation. The causal fungi have been identified as *cryptococcus neoformans* or related hyphomycetes (torula histolytica or torulopsis minor Lodder) Accordingly one may find Busse-Buschke's disease reported as cryptococcosis or "torulosis"

Gilchrist's blastomycosis is a chronic infection caused by *blastomyces dermatitidis* There are two clinical forms a cutaneous and a systemic form The cutaneous form is more common and may develop in any part of the skin, occasionally including the genital region. Montgomery demonstrated blastomycosis of the genital region with destruction of the scrotum. The initial lesions are pustules with central crusts and with miliary abscesses in the marginal zone Larger lesions of a serpiginous pattern present elevated *undermined walls of a livid red color Verrucous forms, simulating tuber* culosis verrucosis cutis, are also observed. Pain is not a constant feature Fever is uncommon in this form of North American blastomycosis.

More serious infections lead to slowly progressing disseminated eruptions and to systemic infections. Systemic blastomycosis may begin as a pulmonary infection subsequently spreading to other organs including the brain and bones. A fatal issue is the rule even in treated cases of gen eralized blastomycosis. Autopsy reveals abscesses in most of the organs, always containing masses of fungi

Histology: Gans distinguished three characteristic tissue changes in European blastomycosis a central necrotic zone containing masses of hyphomycetes a middle zone with polymorphonuclear leukocytes inter *mingled with cellular detritus and lymphocytes and finally epithelioid and* giant cells in varying number The fungi become less abundant toward the peripheral zone, which may be free of hyphomycetes but shows an intense tissue proliferation and frequently a marked tuberculoid structure. In other cases the tissue changes may be limited to granulomatous or myxomatous processes harboring numerous fungi.

In lesions of Gilchrist's (North American) blastomycosis, especially in verrucous lesions, epidermal changes dominate the histological picture, showing acanthosis, hyperkeratosis and intraepithelial microabscesses. An intense inflammatory tissue reaction with findings of budding fungi (blastomyces dermatitidis) completes the picture. Fungi are found also in the miliary abscesses.

In surface infections, masses of hyphomycetes are accumulated *in the* upper part of the cutis, especially in the papillary bodies.

Obviously the varying histological structure depends largely upon the individual defensive power of the patient, as has been demonstrated in other chronic infections such as tuberculosis or syphilis (Ramel, Jadassohn, Gans, *et al.*)

The *differential diagnosis* of cutaneous blastomycosis involves chiefly the exclusion of tuberculous ulcers, the verrucous form of tuberculosis, and occasionally sporotrichosis or vegetating forms of late syphiloma. Bacteriologic examination of pus collected from the minute abscesses in the marginal zone or of smears taken from the ulcers, is of essential importance. Identification of the organisms by culture is indispensable and is moreover of aid in differentiating the European from the North American forms. A positive reaction to an intracutaneous injection of 0.1 cc. of a heat killed autogenous specific fungus vaccine (maximum erythematous reaction within twenty four to forty-eight hours) and complement fixation tests may corroborate the diagnosis in a given case.

Treatment: Stilbamidine (4,4-stilbenedicarboxyamidine) was found by Curtis and Harrell to be effective in the treatment of blastomycosis. This substance is an aromatic diamidine and is related to diethylstilbestrol, but its action appears to be chemotherapeutic and not hormonal. It has proven effective in both the local and systemic type of blastomycosis due to blastomyces dermatitidis.

According to Callaway, cryptococcosis and histoplasmosis may also respond to this form of treatment.

Coccidioidomycosis

Coccidioidomycosis (San Joaquin disease, California disease) usually manifests itself primarily as a pulmonary affection with symptoms resembling those of influenza or bronchopneumonia. The condition may be transitory or when spreading to other organs, to the lymph nodes and skin, may run a fatal course. Cutaneous coccidioidal granulomas develop in both primary and disseminated coccidioidomycosis. The skin lesions include erythema nodosum like nodules, papules, pustules, verrucous lesions and fungating ulcers. Coccidioidomycosis occurs rarely as a localized lesion in the anogenital region.

Coccidioidomycosis as an isolated genital lesion has recently been described by Weyrauch and his co-workers. In two cases, a granulomatous growth involving the scrotal skin, was observed in association with coccidioidomycosis of the epididymis. Culture revealed the causative organism to be coccidioides immitis. In both instances, the condition had earlier been mistaken for tuberculous epididymitis and had necessitated surgical removal of the testis and epididymis in one of the patients. In the first case, the right scrotal and inguinal areas were occupied by a large granulomatous mass which had developed gradually following epididymectomy. The complement fixation test was strongly positive. In the second case, acute post traumatic swelling of the scrotum was followed

by two incisions. The operation revealed a granulomatous mass replacing portions of the left testis and epididymis.

Therapy: Coccidioidomycosis does not respond to penicillin or streptomycin Intensive treatment with sulfathiazole or sulfadiazine proved beneficial in several cases Surgery and roentgenotherapy have been ad vocated in cases in which iodide therapy proved ineffective.

Actinomycosis of the Genital Region

For a long time, actinomycosis in the genitoanal region was reported merely as a rare complication of intestinal actinomycosis In almost all case reports the secondary character of the cutaneous lesion was confirmed clinically or by autopsy

However unequivocal instances of *primary* actinomycosis of the genitals have been observed. Although such reports are very rare, they are of diagnostic importance Most of these lesions were erroneously inter preted as being of syphilitic or tuberculous origin until suppuration of the primary indurated lesion led to bacteriological examination of the pus, which disclosed the actinomyces granules Such a development might, however take weeks or months with all therapeutic efforts proving futile in the meantime.

Clinical symptoms: A painless solid nodule of bluish red color forms at the site of infection, or a stone-hard infiltration will be found as the first manifestation of a chronic inflammatory process which slowly progresses with a marked tendency to softening, suppuration and fistula tion. Gradually the morbid process forces its way into the surrounding tissues. There is little or no pain and there may be little evidence of in volvement of the inguinal glands which may in some instances, however enlarge to form a compact tumor with eventual softening and abscess formation.

Spreading from the primary lesion in various directions, the infectious process may involve the penis, scrotum or vulva, including the surround ing perineal and perianal areas, and occasionally spreading to the *vaginal* tract.

Rauber described primary actinomycosis of the *penis* beginning as a hard circumscribed lesion. Thoroughly resembling an initial syphilitic sclerosis, it was treated accordingly But antisyphilitic therapy failed and serological tests remained negative. Subsequently peripheral pustules developed, harboring actinomyces granules. *Histologically* the primary nodule showed a tuberculoid structure with numerous micro-abscesses. In a similar case, reported by Smith, diagnosis was not possible for two months. The primary lesion on the coronal sulcus was followed by a firm

infiltration on the root and an ulcer on the shaft of the penis The dorsal lymph cord was indurated. The patient's wife remained healthy in spite of marital life

Kohler reported primary actinomycosis of the *scrotum* developing as a solid infiltration in the middle of the scrotal raphe in a man of sixty five years who was engaged in transporting straw and barley for a brewery He had been suffering from intertrigo of the inguinoscrotal folds. The intertrigo was cured, but the bean sized subcutaneous nodules persisted and gradually increased in size Progressing downward the inflammatory process produced additional nodules and a mole-hill shaped tumor expanding toward the anus and over the vasa deferentia. A malignant process was suspected and radical extirpation was performed. Finally recovery took place following large doses of potassium iodide and Roentgen irradiation of a small relapsing nodule in the scar

Primary actinomycosis of the *vulva* is very rare. Significant is a report of Bongartz, who observed a country woman complaining of hard swelling of the labium majus. After three months, the tumor became annoying due to perforation and continual oozing of pus. Actinomycetes were identified in smears and culture After ten months of repeated incisions and curettage, healing was obtained.

Mode of infection: In the majority of cases, primary actinomycosis of the genital region could be traced back to contact infection from fungus harboring material (hay straw or other packing material) Small abrasions thus produced or pre-existing intertrigo furnished a portal of entry K. Tietze reported the casual transmission of the fungus into the vagina by use of an unclean pessary with resulting actinomycosis of the vaginal mucosa.

The *differential diagnosis* includes a consideration of tuberculosis and syphilis, and occasionally malignant growth. The diagnosis depends finally upon the demonstration of the fungus from the sulfur yellow actinomyces granules contained in the pus Failure of antisyphilitic treatment may point to possible mycotic disease.

Therapy: The use of penicillin and sulfonamides (sulfadiazine) has proved effective in several instances of genital actinomycosis Reports are scarce however Large doses of potassium iodide are helpful in some cases. Surgical procedure may be reserved for extensive fistulous genital actinomycosis Roentgenotherapy has been suggested for lesions that fail to respond to other treatment.

Sporotrichosis and Related Fungous Infections

Reports of primary infection of the external genitals with sporotrichum Schenckii or its variants are very scarce as compared with those on

sporotrichosis in other parts of the body surface. However primary infection of the genital region may not be so rare as it might seem to judge from the literature.

Especially in the genital region, the primary lesion i.e., an inconspicuous red papule or pustular nodule forming at the portal of entry may remain undetected for a long time until more significant lesions attract the attention of the patient. Upon questioning, the patients usually date the onset of symptoms several years back, so that when coming for treatment the chronic dermatomycosis is in an advanced stage A disease



FIGURE 14. Sporotrichosis, scrotum. (Dermat. Clinic, Frankfurt, courtesy of Prof Dr O Gans.)

as polymorphous in its cutaneous symptoms as chronic sporotrichosis, will easily be misinterpreted.

Spreading by way of the lymphatics, the infectious process gives rise to a large variety of skin symptoms, such as papules, pustules acneiform efflorescences, or ecthyma and trichophytosis-like lesions. Also verrucous changes occur and most frequently subcutaneous indurations with a tendency to ulceration and invasion of the muscles and occasionally even of the bones.

The lymphatics and the regional glands may or may not show clinical changes. Occasionally cord-like indurations of the larger lymphatic vessels and more frequently glandular hypertrophy have been reported.

Lesions of the mucous membranes may be found in association with cutaneous symptoms (case Hodara, 1923 sporotrichosis of the genital and perianal skin and, in addition, of the oral mucosa, in a fifty year-old woman)

Koschewnikow described *primary* sporotrichosis of the *penis* in a millworker Grayish brown patches formed on the glans, followed by weeping erosions crusts and scaling, with edema of the prepuce. An erosion of the prepuce due to intercourse was believed to be the portal of entry Sporotrichosis was diagnosed by culture and agglutination tests Local treatment proved futile. Treatment with large doses of potassium iodide was followed by complete recovery

Systemic sporotrichosis resulting from primary cutaneous infection appears to be very rare On the other hand, cutaneous eruptions are not uncommon in systemic sporotrichosis derived from primary infection of the intestinal tract

Etiology: Sporotrichosis has been described as "une nouvelle mycose by de Beurmann and Gougerot. (1909) Various hyphomycetes have been described as causal organisms Today opinion prevails that all the strains described including sporotrichum de Beurmann sp Gougeroti, sp aster oides etc are variants of one hyphomycete, i.e., sporotrichum Schenckii. For detailed information the reader is referred to the *Manual of Clinical Mycology* by N F Conant and his associates (Philadelphia, Saunders 1945) and to the recent paper of Young and Ulrich in *Arch Dermat & Syph.*, 1953 (Jan) Stable boys caring for sick horses have been known to con tract the infection Infections of workers could be traced back to con tinual contact with packing materials or with grain (millworkers)

Histology: Sporotrichosis produces rather characteristic changes. Even though not decisive for differential diagnosis, they may be of supportive significance Since the report of de Beurmann and Gougerot, three strata typical of the structure of sporotrichotic nodules have been distinguished namely (a) a peripheral zone with a marked inflammatory reaction of the connective tissue with a chiefly perivascular infiltration (b) an inter mediate zone showing epithelioid and giant cells and (c) a central zone containing micro-abscesses with various degrees of necrosis and polymorphonuclear cell infiltration (Montgomery Gans *et al*) Thus, part of the histological changes are syphiloid and another part tuberculoid in appearance. The different strata, however are not very distinctly separated from each other

Differential diagnosis: The distinction from syphilis and tuberculosis is paramount. The differentiation may be intricate unless concomitant cutaneous symptoms such as pustular ecthyma or trichophytosis-like

efflorescences in the vicinity of the nodules, or ulcers suggest a possible mycotic infection. The prolonged chronic course, the protean cutaneous symptoms and the failure of attempted treatments would support such an assumption Demonstration of the fungus by cultures obtained from tissue shreds is imperative. Mycelia are not always demonstrable in the pus or tissue, and if so only in the deeper tissue layers. Spores, however are well demonstrable by staining. Agglutination tests and complement fixation will confirm the diagnosis.

Therapy: Up to the present time, treatment with large doses of potassium iodide has remained the therapy of choice. It should be given by the rapid method, beginning with a small dose, and gradually increasing up to the moment of evident response This optimal dose should be continued up to the time of complete recovery and for four to six weeks thereafter

Available reports on the efficacy of antibiotics (penicillin, aureomycin, terramycin) will not suffice for any definite evaluation of this form of treatment. It appears that results obtained to date have been less satisfactory than those following administration of large doses of potassium iodide. However their administration may be helpful in cases of a marked intolerance toward iodide preparations

An additional local treatment for sporotrichotic lesions includes dressings with 2 per cent potassium iodide solution, or application of an ointment containing pure iodide 0.2 potassium iodide 2.0 lanolin 18.0 Gr and olive oil 2.0

Hemisporosis

Hemisporosis, first described by Gougerot and Caravan (1906) is caused by infection with a related hyphomycete (*hemispora stellata* Veuil leman) and produces polymorphous cutaneous symptoms similar to those observed in sporotrichosis. Also this fungous infection responds promptly to potassium iodide.

Histologically hemisporosis presents analogous features to those described in sporotrichosis, including the characteristic structural arrangement in three strata.

De Beurmann Clair and Gougerot described hemisporosis of the *dorsum penis* a gumma-like ulcer previously vainly treated with anti syphilitics, disappeared after administration of 4.0 gm of potassium iodide daily In most of the reported cases nodules and subcutaneous indurations dominate the picture

A comprehensive study of hemisporosis, including a review of the literature, has recently been published by D Janke (1950)

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CHAPTER 5

DISEASES OF THE GENITAL REGION DUE TO ANIMAL PARASITES

Phthiriasis (Pediculosis Pubis) Scabies

Phthiriasis (Pediculosis Pubis)

Among the epizoa settling down on the human skin, the *crab-louse* (phthirius inguinalis so-called pediculus pubis or morpion Fr.) is one that prefers the pubic area and the hairy parts of the anogenital region to other areas of the human skin. From this region the parasites may find their way to distant hairy parts, such as the sternal and axillary regions, the legs, and exceptionally the eyebrows, but these are rarely the primary site of infestation. Isolated phthiriasis of the eyebrows and lashes occur occasionally in children and adolescents prior to the appearance of the sexual hair.

The first symptom noted by the patient is *pruritus*. Itching increases gradually as the epizoa multiply. Scratching leads to excoriations, follicular eruptions or pustular eruptions due to secondary infection. In addition, self treatment with insecticides or with mercury ointment may provoke a drug dermatitis overlapping the cutaneous symptoms of phthiriasis.

Transmission may take place during intercourse or by close contact with infested clothing or bed-sheets.

The crab-louse is coarser than the body-louse. Its trapezoid shape does not show the waist like indentation that is seen between the thorax and abdomen of the body louse. The parasite sticks firmly to the hair and is found head-down close to the follicle. Of its three pairs of legs, it uses only the legs on one side of its body to cling to the hair whereas the head louse uses all of its legs. The eggs (nits) with their chitin sheaths are very similar to those of the head louse. The male is somewhat smaller than the female.

Differential diagnosis: The demonstration of the louse and its eggs eliminates any doubt as to the cause of the lesions. The nits persist following destruction of the parasites and remain for a long time as evidence

of previous louse infection. Their initial location close to the hair follicles advances with the growth of the hair

Other residual symptoms include the bluish bluish-gray or blackish lenticular maculae distributed over the lower abdomen and the groins (maculae ceruleae "taches bleues of the French nomenclature) The color of these residual spots is sufficiently characteristic to be distinguished from the more reddish hue of possible concurrent syphilitic roseola Examination under natural light is imperative, since artificial illumination may mask the color of the maculae The bluish dye is derived from the body of the louse and is probably excreted by its salivary glands and transferred to the victim by the bite of the parasite. Exceptionally a differentiation from macular exanthemas other than syphilitic, may become necessary as for instance from the roseola of typhoid fever

Treatment Most of the antiscabetic drugs are effective in phthiriasis, in particular benzyl benzoate solutions pyrethrum etc. After delousing, an auxiliary treatment for scratch effects or pustular eruptions is rarely necessary

Scabies

Not infrequently the first manifestations of scabies appear in the genital region In many cases, transmission occurs by sexual intercourse. However by any route of infection, the acarus scabei gives rise to a general eruption with burrows in the areas of predilection such as the hands and fingers in the axillary and umbilical region and in the genital area. Typical burrows are frequently seen on the penis and scrotum

Continuous scratching may change a scabetic efflorescence of the genitals into an infiltrated nodular lesion that may suggest a concurrent syphilitic infection transmitted from the same partner Dark field examination and a follow up observation may clear the situation before the possible appearance of other symptoms of a venereal infection.

The treatment of scabetic lesions of the genital region does not differ from the general therapy of scabies as described in dermatological textbooks.

NONVENEREAL DISEASES OF THE GENITALS RELATED TO FILTERABLE VIRUSES

Common Warts, Condyloma Acuminatum
Molluscum Contagiosum
Herpetic Eruptions
Vaccinia
References

Common Warts, Condyloma Acuminatum

The pointed condyloma belongs to the group of infectious (benign) epitheliomas of viral origin including the common warts verrucae planae juveniles, filiform warts and the highly infectious papilloma of the larynx encountered chiefly in children.

Etiology: The infectious origin of warts has been doubted for a long time. The findings of basophilic inclusion bodies in cell elements of warts led to the assumption of a filterable virus as a possible causal agent (Lipschütz, Serra, U J Wile and L B Kingery *et al.*) The definition of the various forms of warts as products of a viral infection is now well established.

Transmissibility: Clinical experience has demonstrated the transmissibility of warts by (1) the appearance of warts on excoriations in pruritic dermatoses (2) their simultaneous presence in members of the same household (3) the development of warts on the hands of physicians, following injury contracted during curettage of warts and (4) the transmission of warts (condyloma acuminatum) from husband to wife and vice versa in young married couples (Jadassohn Biberstein, Waelsch)

The *experimental* reproduction of warts was first demonstrated by Jadassohn in 1894 and 1895 He implanted small wart particles into superficial skin tunnels of the epidermis. Warts of the same type formed in thirty-three out of seventy-four implantations. The incubation period varied from six weeks to five and eight months. Similar results were obtained by other investigators using bacteria free filtrates from suspensions of ground wart particles

Serra succeeded in transmitting condylomata from the suprapubic

skin to the patient's and his own hands out of six autoinoculations, two were positive and of six inoculations in the patient, four were positive

E. V Ullmann prepared an inoculum from particles of a laryngeal papilloma. He inoculated his own upper arm, and at the same time, the vaginal mucosa of a bitch Papillomatous warts resulted at the sites of both inoculations following an equal incubation period of three months. The lip of the child operated upon for laryngeal papilloma, had been hurt during curettage Flat warts developed at the site of injury then spreading to the face E. Frei, employing a filtrate from condyloma, obtained flat warts at the site of inoculation.

From these and other reports it may be concluded that experimentally produced warts will not necessarily show the type of the original wart.



FIGURE 15



FIGURE 16.

FIGURE 15 Verrucae planae, perianal.

FIGURE 16. Condyloma acuminatum, destructive form. (Dermat. Clinic of Univ of Naples, Prof Dr M. Monacelli.)

The concept prevails that there may be a common virus responsible for the different types of warts, but that the particular structure of the epidermal base may modify the clinical form in an individual case In other words the virus is the causal agent of warts while the terrain determines the morphologic type of the warts

In all experimental reports a long incubation period extending from several months up to one year is significant.

Analogous results were obtained in serial transmissions of warts from animal to animal of one species. Transmission from one species to another or from animal to man however still remains an open field for further investigation in view of the scarcity of conclusive results available to date. Attempts to transmit human warts to rabbits for instance, have been

futile also in our own experiments conducted with suspension from common warts and from laryngeal papillomata. Similar negative results have been reported in attempts to transmit human warts to monkeys. Special attention, however should be paid to the inoculation results obtained in three monkeys by R. G Green and his associates (subconjunctival injection of ground material from a benign wart like papilloma of the eyelid of a seventy three year-old man)

Incidence, sex and age: Condyloma acuminatum occurs in both sexes at any age. It is most frequently found in the first decade of adult life, predominantly located in the anogenital region, but occasionally on other parts of the skin, especially in moist areas (axillary umbilical, inguinal regions) Its extragenital incidence and cases in children and in virgins, prove that the transmission of condyloma acuminatum is not necessarily related to sexual contact. Intercourse is one but not the only mode of transmission. There is no etiological relation between venereal diseases and condyloma acuminatum, notwithstanding the occasional coincidence of gonorrhea or chancre with the condylomata.

Clinical features: Condyloma acuminatum commences as a pinhead sized, reddish, or in moist areas, whitish minute elevation Growing rapidly it forms single or multiple pedunculated and flat proliferations. Single tumors may reach the size of a strawberry or even of a fist. Multiple condylomata frequently coalesce into cock's comb- or cauliflower like forms They propagate exuberantly under the influence of friction, heat, sweat, uncleanliness or after irritation by urethral and vaginal discharges Then, they become soft and friable. Maceration leads to a malodorous secretion, which penetrates into all interspaces. Among the abundant bacterial flora there may be certain spirochetes, which formerly were mistaken for the causal organisms.

Sites of predilection in the *male* are the inner sheath of the prepuce, the glans, including the urethral meatus, and the coronal sulcus, where condylomata may grow in such a manner as to form a fringe-like trimming A long prepuce and phimosis, with resulting moisture, are contributory factors. Eventually excessive growth and accumulation of smegma and pus lead to perforation of the covering prepuce, followed by spread over larger areas of the penis.

In the *female* it is most frequently the labia minora, the introitus, the urethral meatus and the vaginal mucosa that are involved. Intravaginal condylomata acuminata occasionally propagate up to the cervix uteri. Condylomata grow excessively during pregnancy Perianal and perineal condylomata acuminata are not infrequent in both sexes.

Histology: Condyloma acuminatum presents all characteristics of an acanthoma. The proliferating prickle cells show edema, and in superficial

layers hydropic degeneration Mitoses are found. There is a slight tendency to cornification The stratum corneum is thin and may be absent at the tips of the proliferations

Lipschütz demonstrated *basophilic inclusion bodies* in the nuclei of the prickle cells and in the stratum corneum of warts and condylomata. These bodies seemed to develop very early and to disappear gradually in older warts The basophilic character of the inclusions appeared more pronounced in warts and condylomata acuminata than in molluscum contagiosum or in herpes simplex.

Etiology: The demonstration of the *virus* by means of the electron microscope is still under investigation. Recently Strauss Bunting and Melnick demonstrated spherical virus like corpuscles in *common warts* and plantar warts removed from the *human skin* The specimens examined, contained eosinophilic intranuclear inclusions and solid or vacuolated cytoplasmic masses in many rete cells. However these virus like particles were not seen in all warts, especially not in old ones. Findings of similar particles in condylomata acuminata have not been reported up to this moment

Differential diagnosis: Condyloma acuminatum differs markedly from syphilitic condyloma by its pedunculated papillomatous and cauliflower like proliferations and its friability Syphilitic condylomata form single button like lesions and coalesce to large flat patches which become hypertrophic, due to irritation by friction and maceration or by a concomitan vaginal discharge Findings of treponema pallidum and enlargement of the inguinal glands may corroborate the diagnosis of syphilis. The lymph glands are not involved in condyloma acuminatum except for an occasional tenderness in the presence of secondary infection.

Distinction of condyloma acuminatum from cancer of the penis: Condylomata acuminata occur chiefly in young persons, whereas cancer of the penis usually affects men of more advanced age. In papillary cancer of the penis there are usually more villous excrescences than in condyloma acuminatum. The more reddish color and a granular appearance of the cancer masses are additional aids in differential diagnosis. The granular aspect of penile cancer is due to pearl like cancer cell aggregations Their presence is of decisive importance

An intricate diagnostic problem arises in certain cases of condyloma acuminatum which clinically closely resemble papillary cancer In 1931 Buschke and Loewenstein called attention to an extensive form of condyloma acuminatum characterized by an infiltrating expansion in all directions reaching down to the underlying tissues, including the spongy tissues of the glans and the corpora cavernosa. Nevertheless the principal structure of the skin remained preserved. There was no atypical cell proliferation and no destructive progression. No cancer cells were found in the intracellular spaces or in the walls of lymph and blood vessels.

On the other hand, reports in the literature show that occasionally in spite of a clinically and histologically benign appearance a condyloma acuminatum may mask the onset of malignancy at a time when even biopsy still presents a benign picture.

Treatment: Total removal of all condylomata is necessary to prevent relapses. Surgery (abrasion excision) and thermo-electric treatment may be reserved for extensive, or otherwise inaccessible lesions as, for instance those located near or within the urethral meatus or on the vaginal and cervical mucous membranes

In all of these cases, *podophyllin* treatment is the method of choice. Podophyllin obviously excels all chemicals and drugs previously used in



FIGURE 17 Infiltrating condyloma acuminatum of penis (Buschke Lowenstein) Courtesy of Prof A. Buschke, Berlin.

the treatment of condyloma acuminatum. The promptness reliability and rapidity of this method speak for themselves. Culp and Kaplan used podophyllin (25 per cent) in mineral oil with almost constant success. A single application was sufficient to cure completely 81.5 per cent of a total of one hundred sixty-eight condylomata of the penis. Eight recurrences were controlled by a second treatment. Sullivan and King recorded 100 per cent cures in eighty four condylomata acuminata after one or two applications of podophyllin in oil (similar results reported by New and Marsh and by other authors) Twenty five per cent podophyllin in sandrac varnish dries quickly and permits better control of the medication.

Podophyllin acts directly upon the proliferating epithelial cells with little effect on normal cells a few hours after application, blanching of the lesions is followed by necrosis on the second or third day there is slough ing of the whole lesion, with total disappearance in the course of four days (Culp and Kaplan)

Spontaneous disappearance of condylomata acuminata following removal of one or several lesions has been reported repeatedly corresponding to the same phenomenon observed with common warts. This incidence and other clinical observations ("satellite warts" grouped around an older wart, verrue mère and verrues filles of French authors) suggested the development of immunization processes during the existence of warts Analogous observations have been recorded after partial treatment of multiple mollusca contagiosa or of granuloma annulare.



FIGURE 18. Condyloma acuminatum, cauliflower type vulva. (Univ Clinic Naples, Prof Dr M Monacelli.)

Biberstein prepared a *vaccine* from suspensions of ground particles of warts and of condyloma acuminata, which was filtered after sterilization at 56° to 60° C Intracutaneous injections of 0 1 cc. were given twice a week with prompt response in the majority of the treated patients Several authors had the opportunity to use the original vaccine of Biberstein and obtained favorable results in several cases as did one of us in two children with common warts and verrucae planae respectively Biberstein suggested *immunotherapy* as an auxiliary method in cases resistant to any other treatment, or in condylomata acuminata or warts in extraordinary locations (subungual and plantar warts)

There remains the much disputed question of a possible response of warts to *psychotherapy* We could find no report dealing with condyloma acuminatum.

On this occasion attention may be directed to a little noticed but not uncommon congenital anomaly of the glans penis, which may simulate the earliest stages of papillomata acuminata. Tiny condylomata, when densely



FIGURE 19 Papillae coronae glandis (Buschke-Gumpert) also known as Hirsuties papillaris penis (Majocchi) (Courtesy of Prof Buschke, Berlin.)



FIGURE 20 Hirsuties papillaris (Majocchi) glans penis. (Courtesy of Prof Dr G B Cottini, Catania, Italy)

grouped in semicircular formation near the coronal sulcus, may resemble the papilliform elevations of Majocchi's "*hirsuties papillaris penis* (Buschke and Gumpert s *papillae coronae glandis*) These lesions are distributed in two or more rows around the dorsum penis close to the sulcus. They do not exceed ½ to 1 mm. in length and are of a pink color

Papillae coronae glandis develop in adult men from embryonically preformed structures They have been defined as phylogenetic residua from our animal ancestry suggesting the prickle-shaped or dentiform formations on the male organ of animals but without the functional significance noted in animals.

Histologically papillae coronae glandis show the normal architecture *of this cutaneous area and do not contain the terminal nerve elements as* observed in animals.

Molluscum Contagiosum

The genital region is one of the common sites for another virus-induced epithelial infection, which, like condyloma acuminatum, presents intracel lular inclusion bodies harboring elementary bodies," i.e. the causal virus.



Figure 21 Molluscum contagiosum penis. (Courtesy of Prof Dr J Jadassohn, Breslau.)

Molluscum contagiosum is transmissible by direct and indirect contact (multiple infections in schools and nurseries common use of towels bed sheets, etc.) It has been transmitted experimentally from one individual to another the incubation period varied from three to six weeks (Wile and Kingery Findlay) H. Pinkus (1933) obtained a positive result, follow ing autoinoculation with fresh molluscum contagiosum material rubbed into cross scarifications on his left forearm. A crop of molluscum contagiosa appeared after two months. This agrees with Juliusberg s earlier statement of an incubation period of fifty days (1905)

The skin of children is especially susceptible Multiple eruptions are common in young children A little girl of five years under our observations

showed innumerable mollusca spread over her entire body including the scalp face, chest, shoulders, hands and genitals. Such general dissemination is rare in adults. When involving the genitals, mollusca contagiosa may be found on the penis, scrotum, the labia majora and the peri-genital skin.

The firm smooth nodules varying in size from that of a pinhead to a pea, appear on the normal skin either isolated or in groups. They may be arranged in rows along pre-existing scratch marks. The nodules are of the same color as the normal skin, or of a pale pink tint, with a characteristic waxen or pearly appearance.

The fully developed molluscum contagiosum is umbilicated, not infrequently showing a minute dark opening in the center of the depression.



FIGURE 22. FIGURE 23.

FIGURE 22. Multiple mollusca contagiosa. (CAMERA, R. *Dermat Wchnschr* 98:281 1934.)

FIGURE 23 Mollusca contagiosa penis, cornified form (CAMERA, R., *ibidem*)

On pressure from both sides, a cheesy or grit like mass is expressed. By compressing this substance between two glass slides, numerous clear oval particles will appear under the microscope. These are the molluscum bodies of earlier nomenclature—a term considered misleading today because it is now used to designate the acidophilic inclusion bodies of the molluscum contagiosum cells.

Molluscum contagiosum may persist unchanged for years, and may sporadically disappear spontaneously leaving no scar Exceptionally densely grouped mollusca coalesce to form larger irregularly shaped wrinkled lesions (molluscum giganteum) Secondary infection may produce acneform or pustular lesions that eventually become detached.

Histology: Microscopic examination reveals an intense epithelial proliferation extending into the deeper layers of the rete This downgrowth

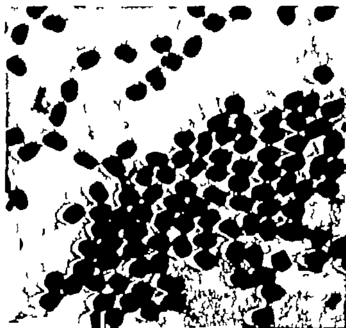


FIGURE 24. Molluscum contagiosum, virus, electron micrograph, magnif × 20 000 (Th. Nasemann, Dermat. Clinic of Univ of München, Prof. Dr A. Marchionini, and Institut f Elektromedizin und Elektronentechnik, München, Prof. Dr W Rollwagen.)



FIGURE 25 Molluscum contagiosum, virus magnif × 34,500, platinum shadowing (Th. Nasemann and W Rollwagen)

originates in the squamous cells of the rete, as well as in the epithelial linings of the hair follicles The proliferating cells appear considerably en larged. The histological picture of a fully developed molluscum contagi osum shows a lobular septated epithelial tumor embedded in the connective tissue of the cutis. Its central area is occupied by the mass described above which is formed by desquamating newformed epithelial cells.

Inclusion bodies: The cytoplasm of the enlarged rete cells presents the vacuoliform cell contents described by Lipschütz (1921) However they are not cavities ("vacuoles) but typical inclusion bodies in the sense of modern virus research They are roundish with distinct membrane subsequently assuming an oval or pear-like shape. These bodies contain the virus corpuscles

The virus was found to be filterable passing through both Chamber land filters and Berkefeld filters. Electron micrographs have demonstrated the brick shaped elementary bodies.

The *differential diagnosis* includes young common warts, small benign neoplasms such as syringoma or hidrocystadenoma, certain nevi and in flammatory nodular lesions of diversified origin.

Very few references are available concerning the possible development of immunologic processes in molluscum contagiosum infections. The pres ence of agglutinins in the serum was not demonstrable in tests of van Rooyen An informative article concerning this phase of the problem has been published by Pinkus and Frisch in the Journal of Investigative Der matology (1949)

Treatment: Manifold methods have proved successful for the removal of mollusca contagiosa. The most practicable method consists in extirpation with a small curette after slitting the center of the nodule. With this simple procedure many mollusca contagiosa can be removed in a single session. In irritable children, it may occasionally be necessary to use an ethyl chloride spray Many dermatologists consider fulguration and electrocoagulation as the method of choice. Very small mollusca contagiosa may disappear following application of a 10 per cent resorcinol ointment which is rubbed thoroughly into the nodules.

Herpetic Eruptions of the Genital Region

Herpes Simplex — Herpes Progenitalis
Herpes Zoster — Herpes Menstrualis
Herpes Virus

Herpetic eruptions are not infrequently observed on the genitals in both sexes. In accordance with the purpose of this presentation, the genital form of herpes simplex, i.e *herpes progenitalis* so-called *herpes genitalis,* occupies first place in our description.

Herpes Simplex

Herpes simplex is a disease entity including herpes labialis, and nasalis, herpetic stomatitis, herpes cornealis, herpes genitalis and herpes urethrae. All of these forms are caused by a common virus. The vesicles of *herpes febrilis* yield identical to that of herpes simplex. Today these two conditions are considered as having the same etiology

Herpes Zoster

Occasionally the genital region may be included in eruptions of *herpes zoster* due to the involvement of lumbar or sacral nerves supplying the cutaneous area of the genitals.

Clinically there are essential differences between herpes simplex and herpes zoster The latter may develop in any segment of the body and, as a rule, is unilateral. Herpes progenitalis is strictly limited to the genitals its vesicular eruption may extend beyond the median line of the body The zoster vesicles are larger than the minute vesicles of herpes progenitalis. Pain is always a marked feature in herpes zoster and may persist for a long time after the cutaneous lesions have disappeared. On the other hand, herpes progenitalis is relatively painless in the majority of cases

The course of herpes zoster is more prolonged than that of herpes simplex, but recurrences, which are common in the latter condition, are extremely rare in herpes zoster

Not infrequently herpes zoster occurs as an epidemic disease in schools camps or barracks, usually during June or in the autumn, but the majority of cases occur spontaneously A similar spread of herpes simplex is unknown.

On the other hand, both diseases present similarities in histogenesis and in cytological findings, thus suggesting a relationship of the pathogenic agents of the two conditions. Both herpes simplex and herpes zoster are virus diseases, although the type of virus in each differs, as will be dis cussed later

In exceptional cases the genital region may be involved in zosteriform eruptions caused by the administration of arsenicals bismuth or certain antibiotics.

Herpes Progenitalis

Herpes progenitalis is found on the glans the inner leaf of the prepuce, the shaft of the penis, and, not infrequently near the mucocutaneous junction of the urethral meatus. In the female it is chiefly the labia majora that are affected, less frequently the labia minora and the clitoris.

Local hyperalgesia, paresthesia and neuralgic pains may precede the

eruption. These prodromal symptoms are neither as constantly found nor as intense in herpes progenitalis as they are in herpes zoster Headache, fever and malaise, all common symptoms in zoster eruptions rarely accompany the onset of herpes simplex. However occasionally more serious symptoms have been described also in herpes progenitalis ("herpes neuralgique of French authors)

Burning and itching accompany the development of one or more groups of minute pinpoint to gravel-sized vesicles in herpes progenitalis. These vesicles may appear either on a normal or a reddened and swollen area of the skin or mucosa. Bursting rapidly the vesicles leave superficial lesions that are soon covered by thin crusts. When neighboring vesicles coalesce irregularly shaped erosions result. Their herpetic origin may be determined by the frequently polycyclic margin



FIGURE 28. Herpes progenitalis.

The inguinal glands, if ever involved in herpes progenitalis, are slightly enlarged and tender on palpation. In most cases, the affection heals within six to ten days in contradistinction to the more deeply seated vesicles of herpes zoster Scars are rarely if ever left by herpes progenitalis, whereas herpes zoster leaves definite scars.

Negligence, secondary infection, or an inappropriate treatment may change the aspect of the herpetic erosions on the genitals, leading to uncharacteristic ulcers, covered with a fibrinous layer or crusts, and these lesions may in turn become changed in such a manner as to simulate venereal infection. As a matter of fact, herpes progenitalis must be considered as a possible forerunner or portal of entry of venereal infection (Sulzberger and Wolf)

Recurrences are frequent in herpes progenitalis usually appearing at the sites of the primary eruption. They occur at intervals of three to six or more weeks but may appear at irregular intervals over a period of years. They are elicited by various factors acting as "trigger mechanisms, as, for instance by the febrile onset of acute infectious diseases (pneumonia, influenza, typhoid or scarlet fever) and occasionally by artificial fever (Sulzberger and Wolf) Sexual intercourse or menstruation may likewise act as stimulating factors.

Herpes Menstrualis

Herpes menstrualis may develop before, during or immediately after the period, and may recur periodically with every menstruation. Menstrual herpes is not necessarily limited to the genital region, but frequently appears as herpes of the lips buccal membranes or elsewhere on the body

Histology and pathogenesis: According to Unna s classic description (1896) the epithelial lesion preceding the formation of vesicles consists of a fibrinous inflammation of the epidermis, with edema and swelling of the underlying papillary bodies and surrounding tissue. The epidermis becomes detached. The walls of the resulting cavity show a coagulation necrosis of the squamous cells. The vesicle fluid contains polymorphonuclears mononuclears, cell debris and, in addition large epithelial cells.

Lipschütz (1921) was the first to describe *inclusion bodies* within the nuclei of the involved epithelial cells in herpes genitalis and febrilis. These bodies may fill the whole nucleus. Experimental and virological research have verified Lipschütz assumption that these inclusion bodies harbor the herpes virus (Lipschutz elementary bodies) These intranuclear inclu sion bodies are eosinophilic, showing a granular structure they are stain able by Giemsa s and other methods. In addition basophile "minute bodies have been described in the cytoplasm of the epithelial cells in experimental meningitis in rabbits as well as in herpes progenitalis in man. Similar elementary bodies have been observed in preparations of cultures from embryonated eggs.

Herpes Virus

The *herpes virus* has been demonstrated abundantly in the vesicular fluid with the aid of the electron microscope. It presents certain char acteristics different from those of any other virus thus far described" (Coriell Rake Blank and McNair Scott, 1950) The virus is found in large amounts in highly infectious, early lesions but is absent in older lesions and in vesicles of other origin. Under the electron microscope virus cor puscles were recognized as rounded bodies of a varying density in the unshadowed preparations In shadowed preparations a central raised area was marked in many bodies. The outline of these bodies appeared irregular and fuzzy

Information concerning our present knowledge of the morphology of the virus its pathogenic properties and the results of experimental research will be found in van Rooyen and Rhodes work on *Virus Diseases of Man* (New York, Nelson, 1948) Part of the following description is based upon the discussion by these authors.

The opinion prevails that the virus of herpes simplex has a tendency to remain in the body producing a "chronic, lifelong infection The virus remains latent, but on stimulation, may regain its virulence to cause recurrences of herpes of the lips mouth or genitals (Nagler) Usually the primary infection appears to occur in childhood, causing a herpetic stomatitis. Significantly the virus of herpes simplex or of herpes febrilis has been detected in the saliva of healthy individuals, transmitted to the rabbit's cornea, it produced herpetic keratitis.



FIGURE 27 Inoculation herpes, thigh. (Lipschutz, B *Arch. Dermat u Syph* *136* 459 1921 Fig. 16.)

The various strains of the herpes virus vary in character Van Rooyen and Rhodes stressed the fact that herpes strains may show both dermotropic and neurotropic properties. Thus certain strains caused meningitis in man, with sudden onset, a rapid course lymphocytosis in the cerebrospinal fluid, and a favorable prognosis. The widely discussed question as to whether the virus of herpes simplex is capable of producing encephalitis lethargica in man appears to have been definitely solved. Almost all recent investigators deny that this form of encephalitis can be caused by infection with the herpes virus.

Lipschütz succeeded in *transmitting* the virus of herpes genitalis from man to man. In one of his experiments, he was able to obtain positive inocu-

lation results in two generations the vesicle fluid being always infectious to the rabbit s cornea. Typical inclusion bodies were demonstrable in the corneal lesions. Mariani obtained positive results, using vesicle fluid for re-inoculation of the same individual. Furthermore, Fontana (1921) was able to reinfect his patient from the rabbit s herpetic keratitis. An incuba tion period of twenty four to forty-eight hours was noted by Lipschütz and other investigators in experimental transmission of herpes simplex from man to man. In the case represented in Fig. 27 the first vesicle appeared on the third day after inoculation additional vesicles around the primary lesion followed during the next three days.

In the course of time, vesicle fluids from all varieties of herpes simplex have been used for transmission from man to man, always resulting in the production of typical herpes simplex vesicles.

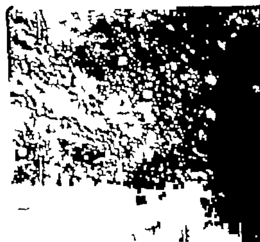


FIGURE 28. Herpes simplex vesicle fluid from lip gold shadowed, magnified × 12,400 (Courtesy of Dr H. Blank.)

The herpes virus is transmissible to various laboratory animals (rabbits rats mice monkeys) In the rabbit, herpetic keratitis is readily produced

The *route of infection* in man is not easily determined in an individual case. Direct or indirect contact with the virus may give rise to infection. As a matter of fact, herpes progenitalis can be elicited or transmitted by intercourse Other instances occur spontaneously Transmission by inter course has been demonstrated experimentally by coupling healthy rabbits with rabbits previously infected with herpes virus by inoculation of the genitals (Mariani Levaditi and Nicolou)

Inclusion bodies and elementary bodies have also been found in *herpes zoster* vesicles the virus obtained, however did not present the biological characteristics of the herpes simplex virus. It does not produce a take on the rabbit s cornea. The extreme rarity of recurrences in herpes

zoster would seem to indicate immunization reactions As van Rooyen and Rhodes stated, no significant immunity is demonstrable in herpes simplex in spite of recurrences However antibodies have been found in the sera of convalescents by investigators using the technic of virus neutralization or complement fixation.

Differential diagnosis: The group vesicles and the rapid course of herpes progenitalis are essential factors in distinguishing herpetic erosions from venereal infections As previously mentioned, it must be kept in mind

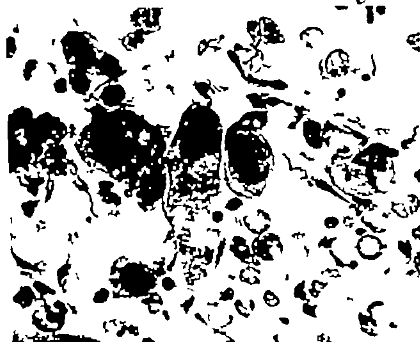


Figure 29 Smear of herpes simplex vesicle, Giemsa stained, magnified × 475 (Dr H. Blank.)

that any herpetic erosion of the genitals appearing after a suspicious inter course, may possibly change to syphilitic chancre or chancroid. Dark field examination is imperative.

Exceptionally a primary lesion of lymphogranuloma venereum may be mistaken for herpes progenitalis. A transient herpetiform erosion on the glans or the coronary sulcus is one of the typical primary manifestations of this virus infection. However as in the nodular form of the initial lesion, the infection spreads rapidly to the lymph vessels, causing the inguinal bubo characteristic of lymphogranuloma venereum.

Other conditions requiring differentiation include eczematous eruptions, drug eruptions, ulcus vulvae actum Lipschütz, aphthous ulcers and

ectodermosis pluriorificialis. The distinction between herpes simplex and herpes zoster has been discussed previously The cornea test in the rabbit constitutes a reliable auxiliary aid in differentiating these two diseases. As a rule the rabbit's cornea does not respond to zoster vesicle fluid in such manner as is typical for herpes simplex.

The rabbit cornea test may also prove of diagnostic value in disseminated cutaneous herpes (formerly Kaposi's varicelliform eruption) a rare condition which exceptionally may spread from or to the genital



FIGURE 30 Infantile eczema, secondary infection with herpes virus.



FIGURE 31. Close-up view of Fig. 30

region. The herpes simplex virus has been detached also in the vesicle fluid of this condition.

Treatment An uncomplicated, non-recurrent herpes progenitalis is a self limited condition and disappears under purely hygienic treatment, supported by the application of mild dusting powders In areas exposed to friction or to vaginal discharge irritation can be prevented by inter position of a piece of lint and by application of boric acid powder Ointments are of less value in the treatment of herpes progenitalis. In more severe cases, aureomycin powder has been found useful in preventing or controlling secondary infection. Systemic treatment is unnecessary in any form of uncomplicated herpes simplex but disseminated cutaneous herpes may require special attention. Baer and Miller judging from their results in two cases recommend a trial with combined systemic and local administration of aureomycin in disseminated herpes

It has been previously mentioned that even though rarely the administration of *aureomycin* may act as a trigger mechanism in eliciting herpetic eruptions. Thus Finland, Kass, and McCracken (1950) reported herpes labialis appearing during aureomycin treatment for herpes zoster and for other infections



FIGURE 32. Primary lesion of lymphogranuloma venereum of one week's duration on coronal glans of penis. (Courtesy of E. R. Squibb & Sons, New York, monograph on lymphogranuloma venereum, p. 18, Fig. III, 1943.)

It is difficult to bring recurrent herpes simplex under control. Judging from the literature, small pox vaccinations, repeated at intervals for six to twelve weeks, are occasionally effective in preventing recurrences.

Vaccinia

Accidental vaccination of the genitals is very rare as compared with vaccinia of the face or the hands, or with vaccinia superimposed upon a pre-existing eczematous eruption (*eczema vaccinatum*) It occurs occasionally in mothers sharing their beds with vaccinated or revaccinated children. Scherber described vaccinia of the vulva and perineal skin in a mother sharing her bed with a revaccinated daughter of ten years of age, who had denuded her pustules by scratching. In drying these wounds with her shirt,



FIGURE 33. Vaccinia, accidental vaccination of penis. (Courtesy of Dr H. Blank.)

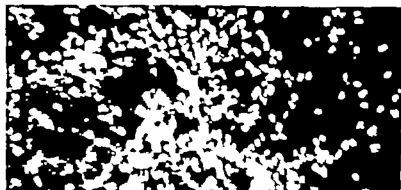


FIGURE 34a.



FIGURE 34b.

FIGURE 34a. Vaccinia virus, prepared from chorioallantoic membrane magnified × 10 000. (D Peters and Th. Nasemann, Tropeninstitut, Hamburg.)

FIGURE 34b. Vaccinia virus, prepared from rabbit's cornea, magnified × 22,500 (Peters and Nasemann)

the mother transmitted the virus to her prolapsed hemorrhoidal nodes and the left labium majus. Another mother after bathing her revaccinated eight year old son, used the water to wash his dressings and to bathe her self and thus contracted vaccinia vulvae

Accidental vaccination of the penis posed a diagnostic problem in a case reported by Coriell *et al.* A boy of three years presented an indurated area on his prepuce with raised margins and a depressed encrusted center The exuded serum inoculated into a rabbit s cornea, produced keratoconjunctivitis, with microscopic demonstration of the basophilic inclusion bodies of the Guarneri type. A positive Paul test (inoculation of the chorio-allantoic membrane of embryonated eggs with the seropurulent contents



FIGURE 35. Eczema vaccinatum of scrotum and penis. (W Konzert u A. Winkler Univ of Innsbruck, Dir Prof. Konrad; *see also Hautarzt*, 5 450 1953.)

of the pustules producing white plaques tending to central necrosis) confirmed the diagnosis.

Accidental vaccination is usually followed by fever prostration and eruption of one or more umbilicated pustules, surrounded by a dark red area, after six to ten days the pustules are heavily crusted. Coalescence changes the clinical picture to larger weeping exulcerations, especially if developing on an eczematous region. Swellings of the regional lymph glands are common.

Recently Konzert and Winkler described eczema vaccinatum of the scrotum and penis superimposed upon an intertriginous dermatitis of the inguinal region, in a twenty-four year old man (Fig. 35) In addition, there were presented the symptoms of transversal myelitis (paresis of the legs retention of urine and stool) Four weeks before, his infant daughter had been vaccinated. All symptoms receded spontaneously within two weeks

following admission. Myelitis in vaccinia is very rare In contrast to the dreaded nervous complications in vaccinated children, myelitis due to vaccinia runs a benign course.

The *differential diagnosis* includes variola, varicella, impetigo and occasionally erythema exudativum bullosum. In contrast to variola vaccinia is never accompanied by lesions of the oral mucosa, but may like variola, yield a positive Paul test. In varicella, however the Paul test is always negative

Therapy: In the treatment of accidental vaccination the prevention of secondary infection is paramount. Penicillin, given by injection will preclude bacillary superinfection In recent experiments Baldridge and Kligman stated that neither aureomycin nor terramycin showed any demonstrable activity against the vaccinia virus itself as measured in the embryonated egg

Very rarely the genital region may be included in *generalized vaccinia*, which is probably due to hematogenous dissemination like in variola. In generalized vaccinia, the mucous membranes (throat, nose) may be involved as in true variola. This never occurs in vaccinia after accidental transmission in connection with vaccination (Mustard and Hendrick)

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APHTHOSIS OF THE GENITALS ECTODERMOSIS EROSIVA PLURIORIFICIALIS AND STEVENS JOHNSON S SYNDROME THEIR POSSIBLE RELATIONSHIP TO ERYTHEMA MULTI FORME EXUDATIVUM BEHCET'S SYNDROME

Genital Aphthosis

The ancient Hippocratic term aphthae (ἄφθαι) has been used to desig nate various solitary or multiple lesions of the mucous membranes of the mouth conjunctivae and genitals.

I Neumann (1895) was the first to direct attention to aphthous erosions of roundish or polycyclic shape of the vulva, vagina and the urethral meatus, concurrent with acute aphthosis of the mouth. Neumann found oral aphthae in eleven of his thirteen patients with genital aphthosis. In addi tion four of these thirteen patients showed skin exanthemas twice of the erythema multiforme type and twice erythema nodosum like eruptions. Subsequently similar syndromes were seen in male individuals. Papulo-vesicular and erythematous lesions completed the picture. Such coincidental occurrences appeared to indicate a systemic infection

Moreover the combination of oral aphthosis with analogous lesions of the eyes (conjunctivitis, keratoconjunctivitis) was repeatedly described in the World literature This ocular mucous membrane syndrome was more *frequently observed during and after World War I In 1917 Fiessinger* and Rendu, comprising their own observations and reports of the literature, described the condition as a well defined disease entity using the term *ectodermose érosive pluriorificielle* This designation has been generally established.

In the United States, Stevens and Johnson (1922) described the con dition as a new syndrome consisting of a feverish stomatitis ophthalmia and cutaneous symptoms. Essentially the syndromes of Fiessinger and

Rendu, and of Stevens and Johnson are identical, the American description referring to a more severe type of ectodermosis pluriorificialis.

Both syndromes are characterized by (1) a feverish aphthous or pseudomembranous inflammation of the oral mucous membranes and of the mucosae of the upper respiratory tract, occasionally involving the lungs



FIGURE 36 Chronic aphthous ulcers of the genitalia in association with oral lesions. (Dermat. Clinic, Frankfurt, Prof. Dr O Gans.)



FIGURE 37 Ectodermosis erosiva pluriorificialis associated with oral and conjunctival lesions, and with nonspecific urethritis. (Dermat. Clinic, Frankfurt, Prof Dr O Gans.)

(2) aphthous lesions of the genital mucosae including the urethral meatus (3) an acute catarrhal or ulceromembranous conjunctivitis with or without lesions of the cornea, and (4) nodular and vesicular eruptions of the genitals, the extremities and rarely on the face In some instances, however cutaneous manifestations may be absent.

The concept of an infectious systemic condition in these cases ap-

peared justified because of the acute febrile onset, an increased sedimentation rate lymphocytosis bradycardia and general weakness as well as the occasional involvement of the respiratory tract. Pharyngitis bronchitis and broncho-pneumonia were found associated with both ectodermosis and Stevens Johnson s syndrome. The form of pulmonary involvement indicated an atypical pneumonia, the infiltration consisting chiefly of mononuclear cells without bacterial findings

For instance, Stanyon and Warner (1945) reported seventeen cases of pneumonitis in association with Stevens-Johnson s syndrome, fourteen of them non bacterial Similar reports of recent time McElfatrick Khajat and Jacoby Kahn and assoc. all of these papers were published in 1950

Notwithstanding the alarming initial manifestations the *prognosis* of these conditions is fair Usually the syndromes disappear spontaneously in the course of one to two weeks. Relapses have never been reported and no *fatalities are mentioned in recent literature. However ocular lesions may* leave lasting damage of the cornea and symblepharon.

Etiology: The etiological problem of ectodermosis erosiva pluriorofi cialis and of Stevens-Johnson s syndrome has not been definitely solved. The well established definition of certain forms of stomatitis aphthosa as viral diseases suggested a possible viral origin also in the conditions under discussion.

In recent times the hypothesis gained ground that both syndromes represent clinical variants of erythema multiforme exudativum The protean manifestations of erythema multiforme occasionally form syndromes in distinguishable from the syndromes described. Today the etiological problem of the conditions under discussion is closely linked to that of erythema multiforme. Stevens and Johnson, themselves, mentioned a possible rela tionship between their syndrome and erythema multiforme.

Dingle in the panel discussion of the Commission on Acute Respira tory Diseases (1946) discussed the increasing number of reports on the coincidence of erythema multiforme exudativum with abacterial pneumonia in the same individual, emphasizing that this type of pneumonia is not a secondary complication but an integral feature of erythema multiforme Robinson and McCrumb (1950) concluded that ectodermosis pluriorofi cialis, Stevens-Johnson s syndrome and also Behcet s syndrome present so many points of pronounced similarity that they should be taken as variants of erythema multiforme exudativum.

It appears however that objections might be justifiable to the inclu sion of Behcet s syndrome in this group This will be discussed later

Inevitably on this occasion, the complexity of the etiological problem of erythema multiforme exudativum comes to light. As a matter of fact also, this question has not been definitely answered. Is erythema multiforme

with all its variants merely a particular form of a cutaneous reaction to a great variety of causative agents? Its interpretation as an allergic phenomenon has been suggested. Or is erythema multiforme a disease entity caused by some specific micro-organism or possibly by a filterable virus?

Concerning the latter question, G Miescher's interpretation of erythema nodosum (1948) will be attractive to those clinicians who still prefer to classify erythema nodosum as a variant of erthyema multiforme rather than as an autochthonous disease In erythema nodosum, Miescher found in the *subcutis characteristic granulomatous structures consisting* of histocytes associated with leucocytes and lymphocytes. These structures usually showed a radial arrangement ("Radiarknötchen," Miescher) or occasionally a palisade-like arrangement of histocytes at right angles to a small central fissure. Miescher considered these histopathologic findings as specific of erythema nodosum.

The *structures were constantly found in tissue specimens* taken from fresh eruptions of erythema nodosum Recently Nube confirmed their presence in twenty out of twenty four cases of erythema nodosum. Miescher concluded that erythema nodosum should be considered as an autochthonous disease of infectious origin. He compared its frequent appearance as a coincidental condition occasionally accompanying infections (tuberculosis, leprosy etc.) with that of the virus-produced herpes simplex which often occurs in combination with venereal infection, acute infectious diseases, *or as a syndrome in drug intoxications (Drug administration to* sensitive individuals may act as a trigger mechanism to elicit an eruption of herpes simplex or of erythema nodosum.) As to a possible virus origin of erythema nodosum, however Miescher refused to commit himself

The *differential diagnosis* includes pemphigus vulgaris hoof and mouth disease Vincent's ulcers, and erythema multiforme exudativum. Pemphigus is a chronic disease with eruptions of oozing bullous lesions ectodermosis pluriorificialis and Stevens-Johnson's syndrome run an acute course. *Vincent's disease produces ulceromembranous and gangrenous* lesions with characteristic findings of fusospirochetosis. Hoof and mouth *disease* transmitted to man mainly *involves the hands* and often *the nails.* Nail changes have never been described in ectodermosis or Stevens-Johnson's syndrome. As previously stressed, a clinical distinction of these two conditions from erythema multiforme will be difficult if not impossible.

Treatment: The fact that the etiology of ectodermosis pluriorificialis and Stevens-Johnson's syndrome is still unknown, explains that treatment has remained *essentially* palliative, with the use of hydrogen peroxide solution as a mouthwash boric acid as a collyrium etc. The results of recent therapeutic trials with antibiotics are contradictory

Sporadic successes in cases of erythema multiforme with aureomycin

seemed to suggest an infectious origin of this affection. Considering ectodermosis, Stevens Johnson's syndrome and erythema multiforme as etiologically related conditions, Khajat and Jacoby Robinson and other dermatologists used aureomycin in Stevens Johnson's syndrome in the cases reported immediate response appeared evident. In other case reports of recent literature aureomycin and other antibiotics proved ineffectual.

The adrenocorticotropic hormone and cortisone have been used with benefit in the treatment of erythema multiforme exudativum. The improvement obtained by steroid therapy in such a self limited disease renders it unnecessary to carry out long courses of maintenance therapy

All efforts should be made to prevent secondary infections of mucocutaneous erosions and ocular lesions by prophylactic administration of antibiotics. D O Wright noted eventless recovery in eight out of nine patients with Stevens-Johnson's disease who had been given sulfonamides or penicillin as a preventive treatment. There remained only one patient who developed symblepharon without corneal damage

Behcet's "Triple Symptom Complex

Behcet's syndrome first recognized by Adamantiades (1930) but exactly described and differentiated from similar conditions by Behcet (1937) differs in many respects from ectodermosis pluriorificialis and Stevens-Johnson's syndrome First of all Behcet's disease is a *chronic relapsing* condition, whereas relapses are unknown in the other two affections. Behcet's syndrome indicates a more serious condition and seems to be an autochthonous disease

Oral and genital erosions (especially scrotal ulcers) and ocular lesions are essential manifestations also in Behcet's syndrome These symptoms may develop in any order The intervals between the various attacks may extend from several weeks to several years Periods up to five and ten years have been noted between first mucocutaneous eruption and the onset of ocular symptoms

Cutaneous manifestations vary from superficial herpetiform erosions to deep crater form ulcers of the scrotum, penis the inner aspects of the thighs and in the female of the labia majora.

Oral lesions consist of about lentil sized erosions but occasionally change to oozing ulcers including the mucosae of the pharynx and larynx. However in contrast to erythema multiforme ectodermosis pluriorificialis and Stevens Johnson's syndrome pulmonary complications have never been recorded in Behcet's syndrome

Ocular lesions in Behcet's syndrome may lead to severe complications sometimes resulting in blindness. Usually the involvement is limited to conjunctivitis, sometimes associated with corneal lesions. These attacks

may run a course of one to six weeks, with or without impairment of vision. Although limited to one eye, both eyes may be afflicted in a later relapse

The most dreaded complication however is iritis followed by hypopyon. In one of two cases reported by Katzenellenbogen (1946) *hypopyon iritis* hemorrhages into the retina and the vitreous occurred in association with *epididymitis* This coincidence, however is most uncommon.

Less uncommon in Behcet s disease is another manifestation, men tioned as an initial symptom already by Adamantiades, namely the involvement of the knee *joints* causing hydrops of the afflicted joint. This incidence has been confirmed by recent authors (Andrews 1946) also periodical hydrops of the same knee joint has been observed recurring with later relapses of the condition.

Behcet s syndrome usually occurs in individuals between twenty and thirty years of age, but may happen at any age. The condition markedly prevails in males.

Etiology: The origin of Behcet s syndrome is unknown. Its classifica tion as another variant of erythema multiforme appears objectionable because, in contrast to ectodermosis and Stevens Johnson s syndrome (a) Behcet s syndrome is a chronic relapsing disease recurring over an indeterminate number of years (b) involvement of the lungs has never been seen in Behcet s syndrome, and (c) because of the more serious type of ocular lesions and their periodical recurrence in Behcet s syndrome.

The concept of a viral infection is hypothetical. Behcet, himself mentioned findings of inclusion bodies and elementary bodies his findings, however have not been definitely confirmed.

Furthermore, there is no evidence to justify the definition of Behcet s syndrome as an allergic disorder (recently again suggested by H Koch) notwithstanding the occasional symptomatic effects of antiallergic prepara tions (Antastan)

Differential diagnosis: The differentiation between Behcet s syndrome and erythema multiforme, ectodermosis pluriorificialis and Stevens-Johnson s syndrome has been previously discussed. The eruptions in pem phigus vulgaris produce oozing ulcers disseminated over larger areas of the body surface. Medicamentous dermatitis runs a self limited course and is seldom associated with serious eye complications.

As previously explained, ocular lesions do not necessarily accompany the initial attack in Behcet s syndrome Years may pass before they occur with later relapses. Genital and oral ulcers as well, forming in Behcet s dis ease may be indistinguishable morphologically from certain forms of *ulcus vulvae acutum* (Lipschütz) Also in this condition concurrent aphthous lesions of the oral mucosa have been occasionally observed. Taken the specificity of bacillus crassus in Lipschütz ulcers as granted, the absence

of this bacillus in smears taken from the genital lesions should speak against ulcus vulvae acutum Lipschütz considered its demonstration as indispensable. However in oral ulcers sporadically seen in cases of Lipschütz ulcers, b. crassus was almost never demonstrable (apparently only by Matras) The reader is referred to Helen O Curth s case report on "abortive forms" of Behcet s syndrome, including discussion (*Arch. Dermat & Syph* 54·481 1946)

Treatment: An effective therapy of Behcet s syndrome has not yet been found. Recently Nelson and Burtness found local therapy of the mucocutaneous lesions with tyrothricin, permanganate, and dilute acetic acid ineffectual. In addition, the lesions progressed in spite of systemic treatment with penicillin streptomycin, sulfonamides, blood transfusion, folic acid, protein hydrolysate etc. Liver preparations proved ineffective in trials by Faaborg Andersen. Brief improvement was obtained by ad ministration of small pox vaccine and pyrotherapy

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CHAPTER 6

NEURODERMATITIS OF THE ANOGENITAL REGION

Introduction
Disseminated Neurodermatitis
Localized Neurodermatitis
Pruritus Ani
Pruritus Vulvae
Pruritus of the Scrotum and Penis
References

Introduction

The increased incidence of cutaneous reactions attributable to nervous factors has frequently been commented upon in the literature. It is obvious that man has not been able to adapt himself to the advances of the machine age. The breakneck speed of modern living engulfs him in a routine that leaves little time for relaxation and recreation Periods of necessary sleep are grudgingly accepted as a time wasting concession to the inherent weak ness of man s physical powers Instead of applying the time saved by modern efficiency and labor saving devices to increase his leisure periods, modern man uses it to increase his output by more work. Under such conditions it is little wonder that cutaneous neuroses have increased. An ex cessive expenditure of nervous energy without replacement by rest, relaxa tion and recreation, must eventually take its toll. Once this deficit of nervous energy reaches a certain threshold, the nerve endings in the skin become irritable and itching results.

The itching may be mild at first but gradually as the irritation of the nerve ends increases it becomes more severe. Scratching of the lesions irritates the skin and inflames it, thus producing superimposed local irrita tion of the already irritated nerve endings In this manner the itching is exacerbated and the impulse to scratch and rub the skin becomes less controllable If at this point, self medication is attempted, it may only too frequently produce still further local irritation After months, and sometimes even years, another factor habit, complicates the process. A nerve pattern is built up which makes it easily possible for the patient to still further traumatize and irritate the affected area by unconscious rubbing and scratching, even when there is no marked itching present. The itching may become so intolerable as to completely unnerve and incapacitate the

patient for social or occupational activities. The neurotic component may thus be of primary predominant or secondary significance, and finally a vicious circle is established each link of which will require careful consideration and special treatment. The patient may be the victim of phobias, with fear of cancer syphilis or infection, or may be in a state of anxiety owing to family or economic problems.

Persons with neurovegetative instability are frequently incapable of meeting sudden or excessive emotional trauma, such as the loss of a relative by death, or the loss of a job In some instances the nervous disturbance acts as a trigger mechanism in producing a cutaneous reaction. It has been claimed by some investigators that patients afflicted with neurodermatitis display various signs of nervous instability including such traits as emotional immaturity naivety sexual frigidity or compulsive work activity Apathy and hostility have also been noted and Sternberg reported a much higher incidence of pathologic encephalograms in such patients as compared with normal controls Anger fear stress and anxiety have all been described in connection with neurodermatitis However normal subjects may also react to sudden strain or shock with neurodermatosis. The complete mechanism of cutaneous innervation is not yet thoroughly understood, but great progress is being made in demonstrating the role played by endocrine metabolic and chemical factors. It is known that the cutaneous blood vessels sweat glands and pilomotor muscles are innervated by the sympathetic system that sweat secretion blood supply and other conditions in the genital region are governed by various physiologic as well as psychogenic processes

In view of the differences in the several forms of neurodermatitis, these conditions are divided here for purposes of convenience into the disseminated type (atopic dermatitis) and localized neurodermatitis. The latter includes pruritus of the various areas of the anogenital region, in consideration of the fact that the regional differences in the tissue and the resultant differences in the appearance of the lesions preclude a typical *manifestation of lichen chronicus simplex of Vidal in these areas*

Disseminated Neurodermatitis

This condition is also known as *atopic dermatitis* and is an inflammation of the skin associated with intense itching, and eventual thickening and lichenification of the skin There is frequently a history of a preceding infantile eczema and the condition is often accompanied by hay fever or asthma. While there is definite psychogenic factor in this disease the patients seem to be especially predisposed to allergic reactions Disseminated neurodermatitis is found predominantly on the face neck cubitals and popliteals and the anogenital areas show involvement only in

severe and extensive cases. Exacerbations are characterized by erythema, edema, oozing, crusting and excoriations with intense itching. As the condition persists the skin becomes thickened dry and scaly and fissuring frequently occurs.

The disease may begin as infantile eczema and then disappear only to recur as atopic dermatitis some years later or there may be a continuous development from infantile eczema to atopic dermatitis.

As involvement of the anogenital region occurs only occasionally it is usually associated with acute exacerbations and therefore there is apt to be edema and erythema, with the edema most noticeable on the penis However severe generalized cases of atopic dermatitis will show chronic involvement of these areas Atypical lesions resembling condyloma lata have been described.

Differential diagnosis: The disease can be recognized from its location and appearance on other areas and the history Therefore there should be no difficulty in differentiating it from other eruptions, such as contact dermatitis

Treatment: The reader is referred to textbooks on Dermatology for the general management of this disease.

For the local care of the affection, starch, oatmeal or bran baths are recommended. The patient should be instructed to refrain from rubbing and scratching the areas. As the eruption is often acute compresses such as boric acid solution or Burow's solution are of value, and a soothing lotion such as calamine lotion can be used to supplement this treatment. In the chronic stage of the condition, which is accompanied by lichenification and occasionally extends to involve the buttocks, thighs and scrotum, relief of itching in older individuals can frequently be obtained by the use of 3 per cent crude coal tar paste. However the anogenital area should be watched carefully for development of tar and grease folliculitis.

Adrenocorticotropic hormone and cortisone produce improvement in many instances. However severe and extensive relapses are noted at times, when the treatment is terminated and sometimes generalized exfoliative dermatitis ensues. These substances can be of value, however if used carefully in selected cases and carefully withdrawn.

Local application of 1 and 2½ per cent hydrocortisone ointment is of value, especially where absorption occurs readily through the thin skin of the anogenital region.

Localized Neurodermatitis

The entity was first recognized and described by Brocq It is also known as lichen simplex chronicus of Vidal, and is typically distinguished by an eruption of patches of thickened skin resulting from rubbing and

scratching areas of intense itching Accentuation of the normal cutaneous striae gives these patches the rough appearance of shark skin. The lesions appear at first to be of a dark pink color but may later turn to a darker brownish color The patches are usually oval in shape and vary widely in size. They may regress spontaneously and permanently or they may recur in the same or other sites The papular lesions present a shiny appearance. Sites of predilection are the nape of the neck in women extensor surfaces of the thighs the anterior and lateral surfaces of the legs and the anogenital regions The dermatitis may be diffuse or circumscribed. The genitals are often the sole site of the lesion but sometimes do not show these typical changes because of anatomic differences in the skin of the region The condition has been variously attributed to nervous endocrine and metabolic disturbances It occurs more frequently in women

Histologic examination of the lesions reveals acanthosis of the epi dermis and occasionally both hyper and parakeratosis in the horny layer The granular layer is only slightly involved, if at all. There is an increase of pigment granules in the basal layer and perivascular cellular infiltration in the corium with lymphocytes, fibroblasts mast cells eosinophils and pig ment cells In the corium, the blood vessels are somewhat dilated and there is some edema in the papillary layer

Differential diagnosis: The shiny papules of localized neurodermatitis may sometimes suggest lichen planus Typical flat topped, umbilicated angular polygonal papules of violaceous hue may usually be found in other areas in the latter condition

More acute eczematous changes in localized neurodermatitis may obscure the true picture In many such instances, it is impossible to dif ferentiate contact dermatitis and other eczematous eruptions. It is only with treatment and further observation that the picture becomes clarified.

Treatment: As acute subacute and chronic stages of the dermatitis are seen in these cases it is best to plan the local treatment appropriate for the special stage encountered as discussed in Chapter 11 on General Principles of Management. In the acute stage of inflammation as evidenced by erythema edema, oozing and crusting compresses of saturated boric acid solution or Burow's solution may be applied for varying intervals, depending upon the severity of the condition During other periods of daily treatment, mild lotions such as calamine lotion will prove of value

In the subacute stage of the inflammation manifested as mild ery thema, some edema, dryness and scaling calamine lotion and a mild zinc paste can be used.

In the chronic stage of the inflammation a stimulating type of oint ment such as 3 per cent crude coal tar in petroleum will prove beneficial.

It is well to remember that tar preparations should be kept away from hairy areas to avoid a complicating tar folliculitis.

If insomnia is persistent it is best to administer sedatives or soporifics. Frequently the sedation achieved by the administration of barbiturates at intervals during the day will enable the patient to sleep at night. Very often a period of rest or change of scene, or removal from the family or even just a change in the daily routine of life may prove beneficial. In very persistent and severe cases psychotherapy may be required.

Pruritus Ani

This term has been used by many authors to apply to any itching condition of the anal region. When used in such a manner the term has a tendency to obscure exact diagnosis. For this reason, pruritus ani has been described here as a sensory neurosis. Although there may be itching only and no outbreak on the skin, there are usually various degrees of edema and inflammation. It is the lesions produced by scratching and rubbing that determine the objective findings. The skin about the anus is usually gray or whitish, but in some cases may be red and shiny. If an eruption develops it may show varying stages from an acute to a chronic eczematous dermatitis. The most typical change is that of localized neurodermatitis (lichen simplex chronicus of Vidal) in which there is a dry scaly red papular eruption on either side of the gluteal cleft in the vicinity of the mucocutaneous junction. The area of involvement may extend entirely around to form a ring in the perianal region spreading over the buttocks to the perineum and even to the scrotum or vulvae. The maceration and infiltration of the tissues leads to accentuation of the anal folds.

Etiology: Although itching in the anal region may be caused by infections, irritants, allergens, parasites including intestinal worms (oxyuris vermicularis) etc. neurodermatitis appears to be the most common cause. Psychiatrists believe that this area is especially likely to become sensitive in patients suffering from anxiety or hysteria but an excessive loss of nerve energy may suffice to produce this result in any normal sensitive subject. The usual neurosis including frustration, grief, hostility, depression, etc. as well as the various phobias have been observed. Psychiatrists have also emphasized the significance of anal fixations, eroticism and homosexual tendencies in relation to pruritus in this region.

Although neurodermatitis is considered as the cause of a large number of cases of itching of the anal region, a certain number will be found to be of *allergic* origin and will respond to exclusion of allergens after all other methods of treatment have failed. Some writers attribute itching in this area to proteolytic substances in the anal exudate.

Histology: The histologic findings will depend upon the stage of the process. During the first period of intense itching there will be little or no lichenification demonstrable clinically even though it may be histologically manifest. In the subacute stage there is both clinical and histological evidence of lichenification. In the third stage or chronic stage there may be secondary changes due to scratching of the lesions or secondary infection The histologic changes are very much like those seen in neurodermatitis. The inflammation of the cutis is not usually severe and is usually perivascular The spongiosis observed in contact dermatitis is usually absent The apocrine and eccrine sweat glands are not involved.

Differential diagnosis: All previously mentioned etiological factors must be considered to pave the way for an appropriate therapy in an individual case. The possible presence of intestinal infestation plays an important part in itching of the anal region of children as well as of adults.

Treatment: In the treatment of pruritus ani, the first step is to remove all irritating factors. Physical and mental rest are important requisites for the success of any treatment. Considerable improvement may follow the substitution of moistened cotton for toilet paper Administration of barbiturates and antipruritic and soothing lotions will help to soothe the patient and to reduce inflammation. In many cases, small doses of Roentgen rays may prove beneficial.

One per cent hydrocortisone ointment is a very valuable aid in the management of pruritus ani. Local applications in a penetrating type of ointment base three or four times daily will often give complete relief even in most stubborn cases within one week.

Pruritus Vulvae

As with pruritus ani this term also is widely used as a diagnostic term often without realization of its true meaning Here too it applies only to itching of the vulvae and therefore is only a symptom. For this reason other causes of itching of the vulva have been excluded from consideration because of the confusion resulting and the symptom is considered as part of neurodermatitis.

In cases of severe itching of the vulvae the appearance of the skin varies according to the stage of the disease In the acute stage the parts may appear swollen and red, with oozing and crusting In the subacute stages the swelling and redness subside somewhat and the skin becomes dry and scaly Finally in the chronic stage the lichenification of Vidal appears with dry scaling and little or no redness, edema, oozing or crusts. Pruritus of the anal region and external genitals are so often associated owing to the proximity of the regions involved that they are frequently discussed together But the special and varied anatomic features of each

of these regions as well as their different aspects in the male and female, require special attention.

Etiology: In pruritus vulvae, as in other forms of pruritus, psychosomatic conditions may be responsible. Drueck has recently emphasized the part played by "necking," prolonged engagements, the reading of erotic literature, erotic movies and frustrated sex life. The condition is rarely encountered in children and seen most frequently in women approaching, or in, the menopause, and in older women. For this reason an endocrine etiology has been suggested, but quite a number of other conditions such as trichomonas vaginalis bacterial infection, pelvic and systemic diseases may play a part and must be excluded before the correct diagnosis can be made. Veit is of the opinion that practically all primary genital pruritus is due to sexual disturbances, emphasizing in particular the part played by the use of condoms, coitus interruptus and contraceptives. It was his experience that psychosexual inhibitions could be demonstrated in 80 per cent of the cases and he emphasized the importance of a psychotherapeutic regulation of sexual intercourse.

Differential diagnosis of itching of the vulva is frequently a difficult problem. Contact dermatitis, intertrigo seborrheic dermatitis and many other conditions accompanied by itching are often classed as pruritus vulvae and in a wide sense of the term certainly can be considered as producing itching and therefore part of this condition However in the strict sense of the word all such diagnoses serve to remove the condition from consideration as pruritus vulvae. The presence of itching without cutaneous changes or other possible causes of itching, would suggest that the sensation arises primarily in the nerve endings of the skin. It seems most likely that such itching is psychogenic in origin and therefore part of neurodermatitis.

Treatment of pruritus vulvae includes the various antipruritic, sedative and psychotherapeutic measures as described for pruritus ani. Hydrocortisone ointment has been of great value in the local management of many of these problems. Many long standing treatment resistant cases have had almost complete relief in one week's use of the 2½ per cent and even a 1 per cent ointment. The more radical interventions such as vulvectomy and nerve block, occasionally employed in very stubborn cases, are mentioned only to be condemned.

Considering the very important psychic component in both pruritus ani and pruritus vulvae psychotherapy ranging from simple psychocatharsis, which is accomplished by merely having the patient confide his problems to his physician to regular treatment by a psychotherapeutic specialist is an invaluable act. One occasionally finds cancerophobia in these individuals.

Pruritus of the Scrotum and Penis

Here as in the anal and vulvar regions multiple etiological factors may be involved, and the exposure of the parts to heat, friction and moisture as well as excretions, supplies a favorable soil for fungi and

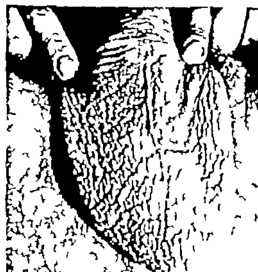


FIGURE 38. Localized neurodermatitis of scrotum and thighs. Note accentuation of scrotal folds and papules of thighs.



FIGURE 39 Localized neurodermatitis of vulva and thighs. (Hudelo, L. *La Pratique Médicale Illustrée* Paris Doin, 1931 Table II Fig. 4)

bacteria. In dermatitis of the scrotum, the skin frequently becomes dry and scaly and scratching leads to the formation of excoriations and fissures frequently complicated by secondary infection Finally the skin becomes thickened and infiltrated assuming a dark reddish brown or brown color

and edema may deform the parts. Like the female genitalia, the male genitals may be the site of a variety of cutaneous eruptions either as isolated lesions in this region or as part of a general dermatitis. It is best to avoid the use of Roentgen therapy in the treatment of scrotal pruritus, owing to the proximity of the sex glands and the danger of producing sterility. However in some desperate cases, in which all other methods have failed to yield relief and in which the special risks involved have been carefully explained to the patient, irradiation may be applied according to the technic described by MacKee and Cippollaro or other authorities in this specialty. Such treatment should always be preceded by a careful report on the condition of the patient's semen so as to avoid possible later medicolegal complications.

One patient was so tortured by pruritus of the penis that he insisted on being circumcised, only to have the itching recur in the scar following the operation.

Differential diagnosis: The differentiation of the neurodermatoses from other cutaneous affections in the genital region is rendered especially difficult by the fact that frequently several different conditions appear together or may be superimposed one upon the other. A careful history may reveal an allergic background, with the characteristic sequence of infantile eczema followed by atopic dermatitis later in life. Examination of the rest of the skin surface may reveal other lesions in areas peculiar to this or that affection, and so furnish the clue to the real etiology of the genital condition. Thus, in psoriasis lesions are very frequently found on the scalp, the finger and toe nails and on the extensor surfaces of the limbs, especially at the elbows and knees. In seborrheic dermatitis the lesions are likewise found in the scalp, but also around the ears, axillae and presternal region and the scales of the latter disease are more yellowish and greasier than those of psoriasis. Once the area has been scratched, secondary eczematization or bacterial infection may develop to complicate the picture, or other conditions such as pinworms or trichomonas vaginalis may be discovered. All of these conditions have their special diagnostic criteria and tests and must be excluded most carefully whenever suspected. Frequently careful questioning may reveal the source of a contact dermatitis from powders, douches, toilet paper, condoms, or other material. The history of exacerbations following emotional or psychic shock may point to a psychogenic origin of the dermatitis.

Treatment: Here, as in pruritus vulvae and ani, psychotherapy may play a very important part. The impulse to scratch has been described as being just as imperative as the impulse to relieve hunger or to seek satisfaction of sexual craving. Frequently the patient scratches the parts during sleep and in his waking hours obtains relief only by increasing the sensation

of itching to one of pain, by scratching The urinary meatus may be involved in the local dermatitis or be traumatized by incessant scratching, and thus lead to painful micturition

The local application, here again, of hydrocortisone ointment is of value and absorption of the medication through the thin epidermis, especially of the penis, permits rapid improvement.

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CHAPTER 7

INVOLVEMENT OF THE GENITAL REGION IN DRUG ERUPTIONS

Introduction
Localized and Fixed Drug Eruptions of the Genital Region
Involvement of the Genital Region in Anaphylactic Reactions to Serum Injections
References

Introduction

The clinical forms of dermatitis medicamentosa are legion. They include erythematous, eczematous vesicular papular acneiform and purpuric eruptions edematous swellings, erythema multiforme-like plaques, and lesions of the mucous membranes. Mixed forms may also occur Any of these eruptions may be generalized or limited to one or more circumscribed areas of the body surface One site of predilection of fixed medicamentous dermatitis is the genital region.

A single chemical or botanical drug can elicit a great variety of cutaneous symptoms independent of the route of administration. Conversely the same type of exanthema can be caused by a great variety of drugs. A patient, unaware of his hypersensitivity to a given drug, may use the compound repeatedly always suffering the same reaction.

No type of eruption is specific for any given sensitizing drug, although certain forms occur more frequently with one, than with another drug One has likewise to consider that the same individual can become sensitive to very different drugs or to groups of related compounds. The search for the sensitizing agent is very complicated because the offending substances may be contained in cosmetic ointments, lipsticks, mouthwashes, dusting powders, in preserves or ordinary foodstuffs, in wearing apparel, etc.

A minimal dose of a drug may suffice to produce an eruption in a sensitive patient. Other individuals receiving larger doses of the same compound periodically or over long periods of time, may not become sensitized until much later Iodoform, formerly widely used in the treatment of chancroid, buboes and infected wounds, was well tolerated in the majority of cases On the other hand, in sensitized patients, clinical

and experimental observations have shown that almost infinitesimal quantities of iodoform powder sufficed to elicit widespread erythematous and eczematous eruptions in the genito-inguinal regions. Solutions of lysol, customarily used for contraception and for vaginal irrigations, may be employed without untoward effects for a long time, and then finally produce outbreaks on the skin

Furthermore the severity of the cutaneous reaction is not necessarily dependent upon the dosage of the drug. The prolonged administration of relatively large daily doses of pot. iodide solution may result in a mild acneiform eruption whereas in other instances the rare and severe form known as iododerma tuberosum fungoides, has been observed to occur even after administration of very small doses of pot. iodide (O Rosenthal) This same phenomenom is observed in the administration of bromides (bromide acne versus bromoderma tuberosum)

Drug eruptions may or may not be associated with systemic reactions such as drug fever headache, vomiting, and occasionally pains and swellings of the joints, reminiscent of the symptoms of serum sickness.

In the following description, we are concerned with certain forms of dermatitis medicamentosa that play an important part in the *differential diagnosis* of nonvenereal diseases of the genitals. The complex problem of sensitization, all details concerning the symptomatology and the management of drug eruptions in general are discussed in textbooks on dermatology and allergy

Localized and Fixed Drug Eruptions of the Genital Region

Aside from the involvement of the genital region in scarlatiniform morbilliform or vesicular dermatitis medicamentosa, we are chiefly concerned with the so-called *fixed* drug eruptions occurring in this region of the body surface. As a rule fixed eruptions reappear at the same spot following each consecutive administration of the causal drug. They are seldom accompanied by the systemic reactions observed in the generalized forms of drug eruptions.

The *penis scrotum and vulva* belong to the sites of predilection for fixed drug eruptions The cutaneous reaction may include the mucous membranes of the vulva, and exceptionally of the urethra.

Individuals sensitized to *antipyrin* frequently present vesicular eruptions and erosions of the genitals associated with similar lesions of the oral mucosa and occasionally with edematous swelling of the eyelids. We observed reddening and edema of the penis and prepuce in a surgeon who had been taking a compound containing antipyrin for attacks of migraine This phenomenon could be reproduced experimentally by administration of the same compound. Shortly following ingestion of

the remedy a burning sensation was felt in the sensitized area. Vesicles formed and developed into painful, oozing and encrusted lesions In all previous attacks healing took place within one to two weeks, leaving a yellowish pigmentation. A few lesions of the buccal mucosa had been observed in earlier attacks.

A classical example of a fixed drug eruption is the isolated erythema multiforme-like patch appearing on the *shaft of the penis* or more frequently on the *fossa radialis of the hand* in patients sensitive to antipyrin. This type of a fixed drug eruption was first described by Brocq (1894) as éruption érythematopigmentée fixe" The fixed antipyrin eruption of the penis leaves a characteristic brown spot, which darkens to a deep black with each subsequent recurrence (verge noire, Fournier)

H. Apolant was one of the first to reproduce this symptom in a sensitized subject. An erythema multiforme-like plaque appeared after each application of the compound. However the same symptoms developed not only after ingestion of the drug, but also after inunction of the sensitized area or of a distant part of the skin with an ointment containing antipyrin.

Clinical experience showed that a fixed drug eruption, although always appearing at the same site of predilection, will not necessarily present the same morphological type following each re-administration but may develop as an isolated macule or a bullous eruption.

The *histological* changes in sections taken from a fixed antipyrin eruption are located principally around the dilated blood vessels which are enclosed in a cloak like mantle of inflammatory infiltrations. Exudation into the tissues is responsible for varying epidermal changes such as spongiosis, vesiculation and parakeratosis (O Gans) A significant change is the increased pigment formation in the stratum basale of the epidermis and in the stratum papillare and subpapillare of the cutis.

Similar localized eruptions occur in patients who are sensitive to the laxative *phenolphthalein* (ex-lax, feenamint, agarol, caroid, etc.) These eruptions are usually located on the genitals, the oral mucosa and in the lumbar region They may also appear as a solitary urticarial or vesicular eruption as an erythema multiforme-like plaque.

Recently H Haber described a fixed drug eruption on the penis in a man of twenty five years, who, in the course of three years, had five attacks evidently due to hypersensitivity to phenolphthalein. Erythematous plaques developed on the glans, usually changing into oozing or en crusted lesions. On several occasions the penile eruption was associated with similar patches on the hands, oral eruptions, and, on one occasion, with scaling lesions of the scrotum. At the same time a slight gray watery *urethral discharge* was noted. This syndrome could be reproduced ex perimentally by administration of agarol which had been used by the

and experimental observations have shown that almost infinitesimal quantities of iodoform powder sufficed to elicit widespread erythematous and eczematous eruptions in the genito-inguinal regions Solutions of lysol, customarily used for contraception and for vaginal irrigations, may be employed without untoward effects for a long time, and then finally produce outbreaks on the skin

Furthermore the severity of the cutaneous reaction is not necessarily dependent upon the dosage of the drug The prolonged administration of relatively large daily doses of pot iodide solution may result in a mild acneiform eruption whereas in other instances the rare and severe form known as iododerma tuberosum fungoides, has been observed to occur even after administration of very small doses of pot. iodide (O Rosenthal) This same phenomenom is observed in the administration of bromides (bromide acne versus bromoderma tuberosum)

Drug eruptions may or may not be associated with systemic reactions such as drug fever headache vomiting, and occasionally pains and swellings of the joints reminiscent of the symptoms of serum sickness

In the following description we are concerned with certain forms of dermatitis medicamentosa that play an important part in the *differential diagnosis* of nonvenereal diseases of the genitals The complex problem of sensitization all details concerning the symptomatology and the management of drug eruptions in general, are discussed in textbooks on dermatology and allergy

Localized and Fixed Drug Eruptions of the Genital Region

Aside from the involvement of the genital region in scarlatiniform, morbilliform or vesicular dermatitis medicamentosa, we are chiefly concerned with the so-called *fixed* drug eruptions occurring in this region of the body surface As a rule, fixed eruptions reappear at the same spot following each consecutive administration of the causal drug. They are seldom accompanied by the systemic reactions observed in the generalized forms of drug eruptions

The *penis scrotum and vulva* belong to the sites of predilection for fixed drug eruptions The cutaneous reaction may include the mucous membranes of the vulva, and exceptionally of the urethra.

Individuals sensitized to *antipyrin* frequently present vesicular eruptions and erosions of the genitals associated with similar lesions of the oral mucosa and occasionally with edematous swelling of the eye lids We observed reddening and edema of the penis and prepuce in a surgeon who had been taking a compound containing antipyrin for attacks of migraine This phenomenon could be reproduced experimentally by administration of the same compound. Shortly following ingestion of

the remedy a burning sensation was felt in the sensitized area. Vesicles formed and developed into painful, oozing and encrusted lesions In all previous attacks, healing took place within one to two weeks, leaving a yellowish pigmentation. A few lesions of the buccal mucosa had been observed in earlier attacks.

A classical example of a fixed drug eruption is the isolated erythema multiforme-like patch appearing on the *shaft of the penis* or more frequently on the *fossa radialis of the hand* in patients sensitive to antipyrin. This type of a fixed drug eruption was first described by Brocq (1894) as éruption érythematopigmentée fixe The fixed antipyrin eruption of the penis leaves a characteristic brown spot, which darkens to a deep black with each subsequent recurrence (verge noire, Fournier)

H. Apolant was one of the first to reproduce this symptom in a sensitized subject. An erythema multiforme-like plaque appeared after each application of the compound. However the same symptoms developed not only after ingestion of the drug but also after inunction of the sensitized area or of a distant part of the skin with an ointment containing antipyrin.

Clinical experience showed that a fixed drug eruption although always appearing at the same site of predilection will not necessarily present the same morphological type following each re-administration, but may develop as an isolated macule or a bullous eruption.

The *histological* changes in sections taken from a fixed antipyrin eruption are located principally around the dilated blood vessels which are enclosed in a cloak like mantle of inflammatory infiltrations. Exudation into the tissues is responsible for varying epidermal changes such as spongiosis vesiculation and parakeratosis (O Gans) A significant change is the increased pigment formation in the stratum basale of the epidermis and in the stratum papillare and subpapillare of the cutis.

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patient to relieve constipation. A few hours following ingestion of the remedy he felt a tickling sensation in the sensitized areas followed by a purplish reddening. Again a slight urethral discharge was observed, con taining some epithelial cells, debris, and a few pus cells.

Such localized eruptions of erythematous and vesicular character have been noted also in patients sensitive to *pyramidon phenacetin* to *barbiturates* and *salicylates*

As previously explained, hypersensitivity may become manifest after every administration of the causal drug by any route whatsoever This does not exclude the fact that some sensitized patients may endure the action of a drug very well after one mode of administration but may react differently following its administration by any other route For instance in the past era of syphilis therapy it happened frequently that syphilitic pa tients tolerated injections of emulsions of insoluble mercury salts without any cutaneous reaction whereas local inunctions with mercurial salves elicited local and sometimes widespread eruptions.

Well known are the erythematous or eczematous eruptions of the genital region following application of *blue ointment* for phthiriasis pubis. In sensitized patients, such a localized eruption may become widespread, involving large areas of the body which did not come into direct contact with the mercury salve

Similar eruptions have been observed in women who use sanitary napkins impregnanted with deodorizing *chlorine*-containing substances In women so sensitized an acute vulvitis developed at the time of each menstrual period.

The local application of tincture of *iodine* or of iodine-containing pow ders and ointments not infrequently results in circumscribed or extensive erythematous and bullous eruptions. Edematous swellings of the penis, prepuce and vulva analogous to the acute swelling of the eyelids or lips following the internal use of iodides, may occur during internal treatment with potassium or sodium iodide solution

Localized erythemas of the anogenital region are not uncommon fol lowing perianal application of *quinine*-containing ointments for oxyuriasis. Also these erythematous or eczematous eruptions may spread over distant parts of the body occasionally resulting in a generalized exfoliative dermatitis.

Owing to the limited space allotted to this description our discussion on drug eruptions on the genitals must of necessity be incomplete Further more we have been forced to omit a description of the acute manifestations of hypersensitiveness to numerous chemical and botanical substances in industrial workers

Of great current interest are the fixed eruptions caused by *arsenicals sulfonamides* and *antibiotics*.

Pentavalent and trivalent arsenicals are known as potential sensitizers, evoking fixed eruptions in certain sites of predilection, including the genital region. Here we would refer briefly to acute erythematous and vesicular eruptions of the genitals in workers in arsenic mines Ledermann reported papulopustular lesions of the scrotum and the thighs, following internal administration of Fowler s solution.

Special attention has been directed to the incidence of fixed eruptions elicited by *arsphenamines*. Chargin and Leifer in an elaborate survey recorded sixty nine patients, all syphilitics, who had fixed eruptions during treatment with arsphenamine (fifty-eight cases) neoarsphenamine (five cases) and silver arsphenamine (two cases) One of the patients developed a fixed eruption also following the ingestion of phenolphthalein. Morphologically *and histologically the skin lesions resembled those of the fixed* antipyrin eruption. Like the latter arsphenamine eruptions leave marked *pigmentations* The lesions are located on the face neck, arms, and legs, and sometimes on the genitals. In Chargin and Leifer s series, the mucous membranes were affected in only one case. Not a single patient developed any of the serious forms of dermatitis medicamentosa when arsenotherapy was continued. Only the local symptoms recurred at the same spot, always and always of the identical type noted previously

This phenomenon was noted most frequently between the tenth and thirtieth days following beginning of treatment, seldom earlier or later and never after the first dose Of the sixty nine patients, fifty-four were negroes and one was of the yellow race.

The sulfonamides belong to the group of drugs capable of causing almost innumerable forms of eruptions in sensitized patients. *Fixed* eruptions although not one of the frequent forms, are mentioned in many textbooks. A check-up of recent literature, however has yielded very few incontestable examples (*one* fixed eruption in a series of five thousand cases of cutaneous reactions due to sulfonamides, Peterkin) Meltzer described a fixed drug eruption of the thumb in a physician who was using sulfadiazine for relief of sinus conditions. The localized eruption could be reproduced experimentally on various occasions, always appearing on the thumb. Following the second administration of the drug the lesion on the thumb was associated with an identical eruption on the *penis*

Penicillin when introduced into clinical therapy was welcomed as a powerful *compound almost* free from untoward side-effects. Subsequently experience proved that cutaneous symptoms are not infrequent, following the administration of penicillin compounds and may be accompanied by systemic reactions such as malaise, headache and drug fever

Today we know that not only penicillin, but any of the antibiotics now available may act as allergenic substances, causing a great variety of gener alized or localized skin eruptions. The most common reaction is the de-

velopment of urticaria erythematous eruptions and especially vesicular eruptions are less frequent A more or less violent pruritus accompanies these eruptions Most serious although rare are localized angioneurotic edemas as untoward side-effects involving the eyelids, lips the tongue, uvula, or the epiglottis also circumscribed edematous swellings of the *genitals* have been noted.

G E. Morris studied twenty cases of anogenital dermatitis following routine treatment with penicillin Erythema, papules scaling and crusts were the usual clinical symptoms. Often such rash extended to the groins, the inner sides of the thighs and the scrotum Itching was slight to moderate many of these eruptions proved resistant to local treatment. Morris found nicotinic acid (100 mg. three times a day given in tablets) most effective in such instances.

Cutaneous reactions to penicillin may become manifest as early as three hours after application, but, on the other hand, may not develop before seven to ten days following discontinuance of treatment (Long)

In addition there occur peculiar trichophytid like eruptions elicited by penicillin compounds Experimental and clinical observations suggest that this type of skin reaction may result from a previous sensitization of the respective individuals to dermatophytes. This phenomenon may explain the occasional onset of a trichophytid like drug eruption immediately following a *first* administration of penicillin.

Cutaneous reactions may occur following any mode of application of penicillin, whether given by local treatment, by injections or inhalations (aerosol inhalation) They are most frequent, however following the *external* use of various antibiotics in salves or dusting powders. Therefore the local application of penicillin is not recommended for the treatment of simple pyodermic affections of the genital region that will respond favorably to other medication Otherwise there is risk of sensitizing the patient and thus forestalling the use of penicillin for some future more serious condition in which the remedy is definitely indicated.

Statistics indicate that skin eruptions occur in about 10 per cent of all cases submitted to penicillin treatment The advanced methods of purification of antibiotic drugs a careful choice of the preparation to be used and proper dosage have greatly reduced but not eliminated the incidence of cutaneous systemic reactions.

In varying proportion about the same variety of drug eruptions has been observed following sensitization to other antibiotic compounds such as *streptomycin aureomycin chloramphenicol* (chloromycetin) *terramycin* and *tetracycline*

The serious systemic reactions occurring during *streptomycin* therapy are discussed in textbooks on antibiotics always with emphasis upon the

incidence of transitory or permanent damage to the eighth nerve with impairment of auditory and vestibular functions as well. Cutaneous reactions have been observed in about 6 per cent of all patients receiving streptomycin over longer periods of time (Long in 2 to 9 per cent according to Waksman) Streptomycin eruptions are usually associated with pruritus.

Peck and Feldman reported a *fixed* eczematous eruption of the groin and scrotum appearing on the eighth day of aureomycin treatment. Recurrence was precipitated by re-administration of the drug

We found no incontestable reports in the available literature referring to fixed drug eruptions following the use of *chloramphenicol* or *terramycin*. In a series of eighty-seven patients receiving terramycin, Finland and his associates recorded only two cases of scarlatiniform dermatitis which promptly disappeared upon discontinuing the drug

Differential diagnosis: Any exhaustive discussion of the differentiation of drug eruptions from other skin diseases would entail a consideration of all important problems of dermatological diagnostics. The polymorphous character of dermatitis medicamentosa explains the danger of diagnostic errors in the absence of any evidence or history of previous drug sensitivity to suggest the origin of the cutaneous symptoms.

The differential diagnosis of localized and fixed drug eruptions of the genital region includes especially syphilis aphthosis, herpes genitalis and eczematous affections of various origin. Weeping infiltrated lesions resulting from a bullous, erythema nodosum-like drug eruption, may be mistaken for syphilitic lesions, especially when located in the genital area, and, in particular in a patient with a history of syphilis Dark pigmented patches on the *penis* resulting from a fixed antipyrin or phenolphthalein eruption may easily be mistaken for the residua of syphiloma.

Vesicular drug eruptions of the *vulva* and introitus must be differentiated from aphthosis. A coincidence with oral lesions is possible in either disease. In both sexes, localized vesicular eruptions may mimic the appearance of herpes genitalis

Localized maculopapular eruptions in the genital region are easily mistaken for simple intertriginous lesions or mycotic eruptions.

There remain only too many instances where, in the absence of an elucidating history the diagnosis can not be made from the morphological aspects alone in such instances of localized drug eruptions of the genitals. In these cases, a careful questioning of the patient is imperative. Patch tests usually render inconclusive or negative results in drug eruptions other than those caused by external application. However an experimental test by re-administration of the suspected drug with due consideration of any risk involved, may yield a definitive clue.

Therapy: The treatment of localized and fixed drug eruptions in the genital region does not differ from the general management of dermatitis medicamentosa. The value of antihistaminic compounds recommended especially for urticarial drug eruptions, the efficiency of BAL in generalized exfoliative drug erythemas the auxiliary local treatment and attempts at desensitization are discussed in detail in textbooks of dermatology

Remarkable relief was obtained in many cases of rashes due to drug hypersensitivity by the use of *cortisone* Newman and Feldman reported total disappearance of all allergic symptoms in a thirty seven year-old man who had received penicillin for three days. There had been edema and erythema of the *scrotum* subsequently expanding toward the inguinal and perineal areas and followed by generalized urticaria. Prompt response to 100 mg of cortisone twice a day for forty-eight hours and, in addition of a total of 100 mg during the following twenty four hours.

The incidence of local irritations of the genital region caused by lysol irrigations or by rinsing or washing with solutions of mercury bichloride has already been mentioned.

Local contact dermatitis following the use of contraceptives of spermatocidal ointments, etc., is not confined to the female sex. Special attention has been directed to the incidence of *penile* lesions following the use of *rubber sheaths* during sexual intercourse (Obermeyer Clarke Rattner) This form of contact dermatitis may be traced to certain chemical substances used in the manufacture of rubber gloves and condoms. Obermeyer reported an intense vesicular dermatitis following intercourse with condom protection. The same patient a physician of thirty-eight years of age, later developed a typical contact dermatitis following the use of rubber gloves the eczematoid eruption increased in intensity with each subsequent use of the gloves finally involving both hands and wrists

Rattner reported an annoying dermatitis of the penis in a dentist Following intercourse with condom protection an intense edema developed, accompanied by some urethral discharge. Patch tests with fragments of the condom were strongly positive. Three weeks later following the disappearance of symptoms, the incredulous patient subjected himself to a test, with resulting recurrence of the edema, dermatitis and urethral discharge.

The possibility of such an origin should be kept in mind in attempting diagnosis of otherwise unexplainable instances of acute penile dermatitis.

The first to furnish a convincing description of an analogous incident in the *female* was C H V Clarke The patient otherwise in full general and gynecologic health felt the first vulvar irritation after resuming marital relations with her husband who had returned from India. At about the same time she suffered some discomfort from a new elastic brassiere.

Patch tests on the patient's back, using fragments of a condom yielded a marked reaction. This case was thoroughly studied. The hypersensitivity was due to the presence of free alkali from potassium oleate used as a stabilizer in the manufacture of condoms Clarke suggested that such a source is possibly a quite common though unrecognized cause in many irritations of the vulva."

Involvement of the Genital Region in Anaphylactic Reactions to Serum Injections

Clinically the cutaneous manifestations of serum sickness resemble those observed in serious cases of medicamentous dermatitis. Edema, urticaria, erythematous eruptions may spread over large districts or may be confined to circumscribed areas of the body surface. Involvement of the genital region in serum exanthemas is not extraordinary Edema of the prepuce the lips, eyelids or face occur usually in association with other cutaneous symptoms. The systemic reactions in serum sickness however exceed largely those occurring in serious dermatitis medicamentosa. Cardiac and renal disturbances and/or acute swellings of the joints are common clinical symptoms in serum sickness.

Experimental research has corroborated clinical experience that the anaphylactic symptom complex never follows a first serum injection a second or later administration is necessary to elicit the manifestations of serum sickness

The occasional onset of symptoms following the *first* application of some allergen suggests a latent formerly acquired hypersensitivity to the respective agent. This may be illustrated by the following example. An acute eruption of edema of the face, the lips and the prepuce developed, following a first injection of a specific horse serum in one of our patients a veterinarian infected with erysipelothrix suis Urticarial lesions, high temperatures, swelling of the knee joints, cardiac and renal disorder complicated the clinical picture. This patient had been occupationally exposed to a frequent contact with horse serum drawn from the animals for the preparation of therapeutic serum compounds.

The *management* of serum sickness is thoroughly discussed in the literature. The prompt response of fever rashes and arthralgia to cortisone has been recently demonstrated in cases of serum sickness.

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CHAPTER 8

OTHER DERMATOSES INVOLVING THE ANOGENITAL REGION

Part I

Eczematous Dermatitis
Intertrigo
Seborrheic Dermatitis
Sulzberger-Garbe Disease
Acne
Edema
Urticaria
Porokeratosis Mibelli
Lichen Nitidus
Psoriasis
Lichen Planus
Pemphigus
Hailey-Hailey Disease

Part II

Xanthomatosis
Scleroderma
Lichen Sclerosus et Atrophicans
Fox Fordyce Disease
Lupus Erythematosus
Hemorrhagic Diseases
Leukemic Diseases
Pseudolues Papulosa Lipschutz
Acanthosis Nigricans
Cornu Cutaneum

References

The arrangement of Chapter 8 has been made chiefly from a practical point of view This chapter is to supplement the dermatoses discussed in a more detailed description in preceding chapters An attempt has been made to give a comprehensive survey here of the great variety of other dermatoses which occur in the anogenital region.

Chapter 8 embraces common and uncommon skin affections which may be located predominantly frequently occasionally or rarely on the skin of this region of the body surface. Notwithstanding their respective frequency they demand equal attention in differential diagnosis and management.

Part I

Eczematous Dermatitis

The term eczematous dermatitis is used here to refer to those eruptions presenting vesicular papular and scaling changes progressing through acute, subacute and chronic stages on the skin.

The term eczema has been avoided. Due to the progress of our

clinical and etiological knowledge the classic word "eczema" has lost its specific meaning Looked at from our present point of view it embraces certain morphologically similar cutaneous reactions to most diversified external and internal irritations nutritional deficiencies, avitaminosis and general conditions such as allergy

The designation eczematous dermatitis may remind of but at the same time is contrasting with the vehemently disputed attempts of an earlier period of dermatology to separate acute inflammatory dermatitis from eczema, especially from its chronic forms.

The acute stage of an eczematous dermatitis is characterized by the



FIGURE 40



FIGURE 41

FIGURE 40 Contact dermatitis, poison ivy Note linear lesions of lower abdomen and thighs.

FIGURE 41 Contact dermatitis, penicillin ointment, perianal region.

presence of erythema, edema vesiculation, oozing and crusting. The subacute stage shows a lessening of erythema and edema, absence of vesiculation and therefore no oozing and crusting The chronic stage presents the picture of lichenification with papules, dryness and scaling and an accentuation of the normal folds of the skin because of increased thickness due to cellular infiltration.

The eczematous changes on the skin may be produced by various types of irritants Even neurodermatitis may present an eczematous appearance in which the irritation is produced by the patient's rubbing and scratching. This is discussed in Chapter 6 on neurodermatitis of the anogenital region.

Contact dermatitis is probably the most common of the eczematous dermatitides, and the anogenital region can be affected by a surprising

number of such irritants in spite of its unexposed position. These may be either primary irritants or allergens. Among the most common of these are reactions to finishes and dyes in underclothing, to condoms, douches and other contraceptives, to finishes and dyes in toilet tissue, to nail polish perfumes, deodorants, hygienic pads. The buttocks may be affected by sensitivity to lacquer or plastic resins of toilet seats. Poison ivy may be transmitted to the anal and genital regions but especially to the external genitalia in the male by contact from the hands. Cutting oils which have saturated the trousers of workers also affect these areas.



FIGURE 42. Lysol burn.

The clinical picture of an eczematous dermatitis varies because of the local peculiarities of the tissue. In response to severe irritation, the penis swells quite readily as does the scrotum. Acute changes affecting the anal region will produce swelling of the perianal folds and the tissue assumes a macerated appearance. The penis and the scrotum can be affected by chronic changes but the scrotum is much more apt to present lichenification.

Histologic picture: The microscopic changes in eczematous dermatitis are nonspecific and vary according to the stage of the condition.

Treatment: The most important feature in the management of these patients is the removal of the offending agent. A careful history will disclose the underlying cause and prompt removal will simplify further treatment. Local treatment depends on the stage of the inflammatory reaction and has been discussed in Chapter 11, devoted to general therapy

Intertrigo

The most persistent and uncomfortable condition affecting the anogenital region is intertrigo. This is more common in Summer time, especially in the obese individual. It appears to be a result of friction on moistened, warm skin in opposing areas where it is thin and delicate Its co-existence with other conditions may be a source of confusion in diagnosis.

At first, there is erythema in the affected area and then the skin becomes macerated. The upper inner thighs are most frequently involved, but the eruption may extend into the inguinal folds and posteriorly to the anal region and the intergluteal cleft. Erosion of the skin may occur with

exudation and severe discomfort of itching or burning, especially in walk ing. As the condition progresses fissuring is a frequent complication, especially in the inguinal folds and the intergluteal cleft. In cases of long duration, even verrucous changes may occur in these areas

Microscopic examination and cultures of the affected areas will often yield yeast or streptococci. Their exact role is debatable. It does sound likely in many instances that the condition begins with miliaria.

Differential diagnosis: Acute dermatitides such as contact dermatitis and neurodermatitis may pose a difficult diagnostic problem. However the history of the condition the location in other areas such as the axillae and inframammary regions as well as further observation of the patient in response to treatment, should exclude these conditions.

Probably the greatest diagnostic importance of intertrigo is the diffi culty which it occasions, when it masks a previously existing eruption. Only treatment and further observation can adequately answer this problem.

Treatment: When the disease is recognized, its management in most instances is rather simple The parts should be kept separated, and a dusting powder containing zinc stearate and talc should be applied. A lotion con taining 5 per cent zinc oxide in liquor calcis usually gives satisfactory results.

Clothing should be loose and light, in order to allow aeration of the area as much as possible. Strapping of the buttocks with adhesive tape can be a valuable adjunct to treatment when the intergluteal cleft is affected, to allow better aeration When the upper inner thighs, in women are involved, a special cloth garment is obtainable which covers each side of the upper inner thighs to prevent friction in walking Obesity a common factor should be treated.

Seborrheic Dermatitis

This disease frequently affects the anogenital region While it is most commonly found on the scalp in the form of scaling dandruff it also is seen in the postauricular regions the frontal region of the forehead at the anterior hair line the eyebrows the alae of the nose the presternal region the middle of the upper back, the axillae, the umbilicus the pubic region and the intergluteal cleft

On the pubic region in the hairy portion it is most apt to present the typical greasy yellow scales of the disease. In the obese individual the inguinal folds and the intergluteal cleft are often affected. On the glans penis, it tends to present a rather superficial, red poorly outlined appear ance The location in this area is frequently subject to irritation by sexual intercourse

In more severe and extensive cases it can involve the entire anogenital

region extending from the pubic region down over the external genitalia, the perineum and to the upper portion of the intergluteal cleft In long standing cases, the skin may become lichenified.

The histologic picture is not characteristic.

The etiology is unknown however exacerbations are not unusual in relation to constitutional diseases or emotional upsets.

Differential diagnosis: Seborrheic dermatitis can readily be differentiated from other diseases affecting this area, when there are typical manifestations of the disease affecting other areas of the body such as the scalp ears, face, presternal region and umbilicus

However when the disease is localized to the anogenital region, the differential diagnosis may be quite difficult if not impossible especially when the picture is obscured by secondary changes of eczematization or intertrigo In such instances, further observation and response to treatment are helpful in evaluation of the disease.



Figure 43 Seborrheic dermatitis.

Treatment: In the acute stages of seborrheic dermatitis moist compresses and lotions are valuable. The application of an ointment at this stage may produce secondary eczematization with further extension of such changes to involve other areas of the body

Sulfur in ointment form is of distinct value in less acute phases of the disease In the subacute stage the sulfur may be incorporated into a paste using 6 per cent precipitated sulfur to a simple zinc paste. In the more chronic stages the 6 per cent sulfur application can be incorporated in an ointment base with little fear of irritation.

Large doses of Vitamin B complex had been advocated. Attention to the general health of the patient is a necessity and concomitant constitutional disease should be treated.

Affected areas on other portions of the body should also be treated.

Small doses of Roentgen therapy are often of value in stubborn cases of the disease.

Sulzberger-Garbe Syndrome

In 1937 Sulzberger and Garbe described nine cases of an exudative discoid and lichenoid chronic dermatosis characteristic enough to be estab-

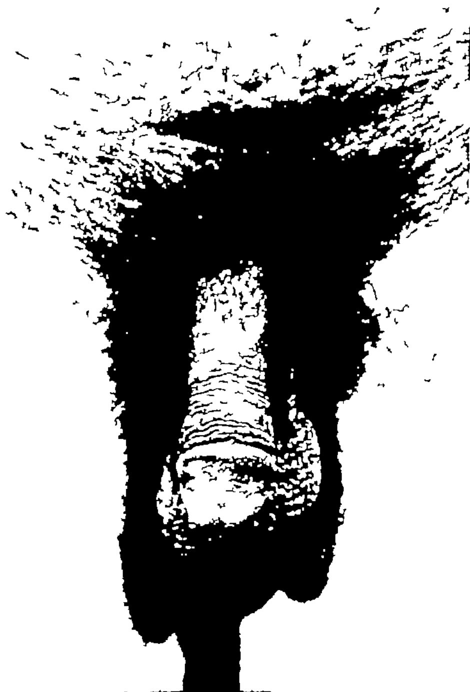


FIGURE 44 Exudative discoid and lichenoid chronic dermatosis (Sulzberger and Garbe) (Department of Dermat. & Syph. of the N. Y. University Post-Graduate Medical School, Dr Marion B Sulzberger Chairman, and the Skin and Cancer Unit of the N. Y. University Hospital.)

lished as a distinct skin affection distinguishable from other types of so-called eczema. The condition is now known as "Sulzberger-Garbe's syndrome" It is characterized by (a) typical discoid and lichenoid elevated plaques (b) a typical persistent exudation and scaly lesions (c) oval scaly lesions with tendency to follow the lines of cleavage somewhat resembling pityriasis rosea, and (d) typical wide-spread lichenification with discrete frequently follicular and lichenoid papules, resembling a "lichenoid id. This condition may involve the genital and perigenital region as can be seen in Figure 44. There are a few fairly characteristic penile lesions and some lichenoid lesions on the thighs associated with several characteristic pityriasis-like lesions on the lower abdomen. Persistence of lesions on the penis is considered to be a common finding

This condition runs an obstinate chronic course with slow response to local therapy Chronicity and the "lack of positive laboratory or other tests support the clinical diagnosis

Acne

The common chronic disease of the pilosebaceous follicles may in unusual instances, be found on the buttocks. This may occur in severe extensive acne eruptions.

Atypical location of acneiform lesions is more frequent in eruptions due to iodine, bromine or chlorine compounds in sensitized individuals. These acneiform lesions may then be associated with nodular or tuberous and occasionally with vegetating lesions Every area of the body including the genital region can be involved.

The treatment of acne vulgaris with atypical location does not differ from that of acne of the sites of predilection (face, chest, back)



Figure 45 Acne, cystic type buttocks.

Edema of the Genitals

The abundant areolar subcutaneous layer and the great supply of blood and lymph vessels of the labia majora greatly promote the formation of excessive swellings of the vulva. Acute edema of the vulva may extend to the vulvar mucosa including the meatus urethrae and the introitus vagina. Likewise the loose connective tissue of the prepuce allows grotesque edematous swellings of the penis.

Edema of the genitals may develop as a part of general edema in cardiac or renal insufficiency nutritional deficiency endocrine disturbances allergic conditions. It may form as a reaction to local infection trauma or chemical injury

The special role of edema in clinical gynecology or in connection with pregnancy is discussed in gynecological textbooks. A condensed survey of G L. Miller (1951) discusses the multitude of causal factors. The sequelae of persisting edema, in particular the various forms of chronic hyperplastic edema (elephantiasis) of the genitals, are discussed in Chapter 16.

The most acute form of circumscribed edema is the so-called *angioneurotic edema* first described by Quincke 1888 Predominantly involving the lips, eyelids, the tongue, pharynx or the fingers, it occurs not infrequently as a circumscribed acute edema of the penis and scrotum. Rapid swelling usually reaches its climax after a few hours to regress within twelve to thirty six hours however it may recur at irregular intervals over a period of many years. The etiology is obscure.

Quincke s edema has been repeatedly observed as a hereditary condition and its location on the scrotum has been known long before the end of the Nineteenth Century (A. F Barnett s quotation of an observation of F A. Mai, Heidelberg 1777 "Within fifteen minutes the whole scrotum was swollen larger than an oxbladder like a monstrous hydrocele)

Osler (1888) reported on a family of thirty-six members with the disease occurring in five generations.

Treatment: Regarding the obscurity of its origin treatment can be merely palliative Recently G A. Hansen (1950) reported rapid regression of Quincke s edema in eight of nine cases after one local injection of hyaluronidase Cortisone and antihistamines are sometimes of value

Urticaria

Urticaria not infrequently affects the anogenital region The usual wheals are not often seen however because of the distensible nature of the genitalia, so that angioneurotic edema is produced Here the swelling occurs primarily in the deeper portions of the skin around the subcutaneous tissue Examination of the remainder of the skin surface will usually disclose some typical wheals of urticaria or edematous reactions affecting the eyelids, lips lobes of the ears or the mucous membranes of the mouth tongue or digestive organs. The hands and feet may be also swollen With edema of the external genitalia, when the penis is affected the overlying prepuce may be so stretched as to be almost transparent Because of this edema there is more apt to be burning than itching In the presence of urticaria, the friction to which the external genitalia are so commonly exposed may cause the rapid swelling of these parts

Urticaria may be due to various causes. It is seen in the presence of many skin diseases such as scabies dermatitis medicamentosa, erythema multiforme, dermatitis herpetiformis, Hodgkin's Disease and leukemia cutis. It is most dramatically seen as a result of ingestion of foods to which the patient is hypersensitive. Exposure to heat, cold sunlight may also be factors in certain instances and psychogenic factors not infrequently play a part.

Differential diagnosis: Edema from any other cause may be confused with the marked swelling of urticaria and angioneurotic edema. Contact dermatitis can produce changes which resemble this but careful examination will usually disclose some evidence of changes on the surface of the skin and usually there will be some evidence of vesiculation oozing or crusting.

Treatment: The advent of the antihistaminic drugs has aided greatly the management of urticaria. These substances given in sufficient dosage will usually produce prompt improvement. The underlying cause however should always be searched for and careful attention to the patient's history in most cases, will uncover the active factor producing it.

Those cases not responding to the antihistaminics are often helped by the use of adrenocorticotropic hormone or cortisone Cold compresses are of value for local relief of the swelling Injections of adrenalin and ephedrine are still useful aids in management.

Psoriasis

The genital and anal regions are more often found to be the site of psoriasis than is usually realized. While not seen here as commonly as on the sites of predilection such as the elbows knees and the scalp it is not infrequently found in the anogenital regions. The designation of psoriasis of this part of the skin as a variant of atypical psoriasis known as psoriasis inversa (psoriasis of atypical location) can only be used with reservation in cases where the genital eruption is part of a general eruption. More uncommon, however are solitary plaques of psoriasis developing and persisting on the glans penis, the labia majora or the intergluteal cleft over an undetermined period, usually most resistant to local therapy The term *psoriasis inversa* has been applied to such locations as the axillary folds, the retro-auricular area, the perigenital region and the flexor aspects of the extremities (Santojanni in Monacelli's monograph on Psoriasis, 1953)

Both the acute type, with tiny bright red, silvery scaled lesions (psoriasis punctata) which enlarges into discs and finally unites into lamellar scaling patches (p guttata, annularis and gyrata) and the chronic, circumscribed form may involve this area. Frequently only the genital region is involved, the residuum of a healed generalized eruption.

In the anogenital district, the areas most involved are the scrotum and penis and less commonly the genitocrural folds. But the psoriatic plaques may spread also to the latter areas, and occasionally to the scrotofemoral opposing surfaces as well. In these areas, if irritation occurs as a result of friction or injudicious treatment or there is super



FIGURE 46. Psoriasis, glans and peri genital region.



FIGURE 47



FIGURE 48.

FIGURE 47. Psoriasis (same patient as Fig. 46)
FIGURE 48. Psoriasis of glans.

imposition of other dermatoses the picture is greatly distorted and diag nosis may be difficult, if not impossible. Consideration of this in diagnosis must be made for therapeutic purposes especially if typical areas of psoriasis can not be found in other areas. These psoriatic patches become inflamed, and there is oozing and crusting followed by the appear

ance of fissures Such fissures occur in the inguinal folds and also in the gluteal cleft and on the penis, scrotum and perineum The margins of these fissures are whitish because of maceration, the result of moisture and friction. There is slight itching under these conditions.



FIGURE 49 Psoriasis in patient with pruritus vulvae showing Koebner's phenomenon with outbreak of psoriasis as a result of scratching.



FIGURE 50 Psoriasis inversa, perianal. (Dermat. Clinic, Frankfurt, Prof Dr O Gans.)

On the penis and inner prepuce, a psoriatic balanoposthitis may develop with absence of scales, but showing definite redness and swelling In such instances, the presence of small red, solitary patches on the glans is often of diagnostic value. Due to the intertriginous irritation in psoriasis of

coal tar emulsion after each washing. Before applying ultraviolet irradiation, the erythema dose must be determined carefully in each case

Ellis recommends a modification of the Goeckerman method, employing liquor carbonis detergens He is of the opinion that the curative action resides in the tar rather than in the direct action of the ultraviolet rays. Chrysarobin and other strong ointments should be applied cautiously in these areas.

Roentgenotherapy has been used locally and should be restricted to cases in which other remedies have proved futile. It must be administered with great care because of the tendency of the disease to recur with damage to the skin and underlying structures following indiscriminate usage The same refers to the use of radium or radio-active substances (Radon, Thorium X)

Autohemotherapy is widely used and recommended. It is quite possible that it has a psychotherapeutic effect. Some writers report encouraging results with oral administration of fresh lard Other recommendations include a fat restricted diet, administration of sarsaponin, massive doses of Vitamin D and preparations containing soy bean lecithin and defatted wheat germ. Arsenic is little used at present, because of the development of arsenical keratoses and epitheliomna with prolonged dosage.

Frequently a change of climate, or a visit to vacation areas may prove beneficial. An attempt should be made to help the patient in his social and emotional adjustments with the aid of psychotherapy if necessary Sedatives and hypnotics may be needed to relieve itching and insomnia, and to prevent excessive loss of nerve energy The importance of nutritional therapy of skin conditions has a special bearing on the exudative form of psoriasis

Adrenocorticotropic hormone and cortisone, while occasionally producing some improvement, are generally not of value especially in chronic cases of the disease These preparations seem of greatest value when secondary eczematous changes are present Local use of hydrocortisone ointment may also be of value in combating such secondary changes.

Lichen Planus

Lichen planus with its characteristic flat topped angular tiny polygonal papules often affects the penis. The disease is commonly found on the flexor surfaces of the wrists forearms and legs just above the ankles and the classical violaceous appearance is usually seen in these areas. The disease is usually chronic but occasionally is seen in acute forms.

Usually the papules on the glans penis are arranged in annular fashion but scattered isolated papules are not unusual. On the shaft of the penis



FIGURE 52. Lichen planus of glans.

FIGURE 53. Annular lichen planus of shaft of penis. (Dermat. Clinic. Frankfurt, Prof. Dr O Gans.)



and the scrotum, the papules are more apt to be scattered and sparse and may be almost invisible in the folds of the tissue.

The color of the papules on the glans varies from purplish-red to white, depending on the presence of moisture. Where the glans is covered by the prepuce and there is resultant moisture, the papules appear whitish while on the exposed surface of the glans the purplish-red color is found. Papules on the vulva have the same appearance as those

Figure 54.

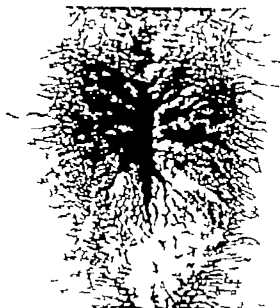




Figure 55

Figure 54. Lichen planus, verrucous type of anal and perianal regions. (Dermat. Clinic, Frankfurt. Prof. Dr. O. Gans.)

Figure 55. Annular lichen planus of scrotum. (Dermat. Clinic, Frankfurt. Prof. Dr. O. Gans.)

on the glans. These color changes undergo the same progression as lichen planus on other areas of the body and eventually become brown.

While itching, as in other areas, is a predominate feature excoriations are uncommon. The acute changes with edema are usually not seen, except as a result of improper treatment and resultant irritation.

The etiology of the disease is unknown but psychogenic factors appear to be important.

Histology: The changes seen in lichen planus are quite typical. There is hyperkeratosis, increase in thickness of the stratum granulosum irregular acanthosis, liquefaction degeneration of the basal cell layer and a band like infiltrate in the upper portion of the corium.

Treatment: Cortisone seems of value in the treatment of this disease but recurrences are not infrequent. Intramuscular injections of insoluble Bismuth also are of value. Attention to the psychogenic aspects of lichen planus seems of definite importance.

Porokeratosis (Mibelli)

Porokeratosis (*Mibelli 1893*) is a rare hereditary skin affection located chiefly on the face neck, trunk and the extensor aspects of the extremities. Its occurrence in the genital area, however is not unknown In 1899 Mibelli himself described a case of porokeratosis with involvement of the glans penis and the oral mucosa. His patient presented cutaneous lesions on the scalp face the hands, thighs, and several typical patches on the glans penis and the scrotum. Typical lesions on the mucous membranes as described by Mibelli, are very rare.

The early eruption appears as distinct superficial, conical elevation of normal, pinkish or yellowish-gray color showing a central comedo-like horny plug. This lesion expands slowly by peripheral progression to form sharply bordered lentil to pea-sized or larger plaques surrounded by a raised keratotic margin, which, like a collarette, encircles the pitted, slightly atrophic central part. At this stage the cornoid" (Mibelli) plug of the initial lesion has disappeared. Such a plaque may persist indefinitely or may slowly grow to form annular gyrate or circinate lesions. Significantly the crest of this collar-like margin, in its total circumference, shows a well defined groove and, along this furrow an adherent thin horny lamella. Spontaneous regression is rare.

Histology: Mibelli's assumption that the condition is closely related to the ducts of the sweat glands has been subject to question from the beginning He was first opposed by Respighi who also in 1893 described this affection as a hitherto unknown hyperkeratosis (ipercheratosi eccentrica) Subsequently Ducrey and Respighi (1898) used the designa-

tion "hyperkératose figurée centrifuge atrophiante. This term approaches our present concept Further studies have shown that (1) the ducts of the sudoriferous glands (the "pores) may be involved but that their in volvement is not essential in the pathogenesis of this condition, and (2) that a parakeratosis rather than a hyperkeratosis dominates the structure of the horny marginal zone Accordingly G Miescher suggested replacing the obsolete name "porokeratosis by the term "parakeratosis centrifuga atrophicans or parakeratosis annularis"

Etiology: There are no reasons sufficient to support Ritchie and Becker s suggestion of a possibly infectious (pyogenic) origin. Heredity factors have been reported in many cases sometimes over three or four



FIGURE 56. Porokeratosis (Mibelli) (Courtesy of Prof Dr R Casazza, Pavia, Italy)

generations. Familial incidence is not extraordinary The interpretation of porokeratosis Mibelli as a nevoid structure remains hypothetical

Differential diagnosis: The condition will seldom give rise to diag nostic difficulties The appearance of the collar like margin with its fine groove will suffice to exclude circinate lichen planus. In addition the histological characteristics should settle the problem

Therapy: Porokeratosis Mibelli has been considered as incurable by expert physicians. Excision or destruction by electrocoagulation was usually followed by relapse or eruptions elsewhere on the body Recently Gottron and also Kimmig achieved what seemed to be a complete cure by repeated applications of thorium X (14 000 electrostatic units divided over five treatments) Response was definite

Lichen Nitidus

Lichen nitidus first described by F Pinkus (1907) is a clinically well defined rare dermatosis of unknown origin. When confined to the genitals

its minute lichenoid papules may readily be mistaken for early lichen planus lesions (miliary form of lichen planus) The shaft and the glans of the penis are the sites of predilection.

In addition, eruptions are encountered on the abdominal and thoracic skin, the arms the bends of the joints, axillae, the dorsal aspects of the hands, with or without concurrent lesions of the genitals. Disseminated lichen nitidus may involve any cutaneous lesion and exceptionally the



FIGURE 57a. Lichen nitidus. (Trimble W B and Maloney E. R *Arch Dermat & Syph* 7 1923.)

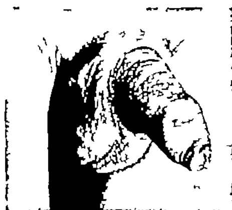


FIGURE 57b. Lichen nitidus in a 7 year old colored boy Courtesy of Dr H. Pinkus, Detroit.

mucous membranes (Pinkus, Arndt, Trimble and Maloney Sutton *et al.*) Recently Barsky and Schorr described lichen nitidus confined to the face.

Lichen nitidus in the female seems to be very rare (one case described by Kyrle) papules in the groins, the genitocrural folds labia majora and axillae in an eighteen-year-old girl. However one should consider the fact that the majority of the patients observed were unaware of this painless, non-pruritic condition, until it was detected casually in connection with some medical examination.

The lesions of lichen nitidus consists of multiple distinct, pinpoint to pinhead-sized, skin-colored lichenoid papules sometimes presenting a dull or semi-translucent aspect. A fine depression may be recognizable in the center of such papules. When located on the glans penis the lesions may

be arranged in groups. But there never develop annular or gyrated forms, as seen in lichen planus of the penis. Lichen nitidus usually persists unchanged over an undetermined time Sporadically spontaneous regression has been noted.

Histology: Lichen nitidus presents a characteristic microscopical picture Biopsy reveals a hemispheric subepithelial granuloma showing a tuberculoid structure, with peripheral lymphocytes, central epithelioid cells and giant cells of the Langhans type Some parakeratosis is seen in the surrounding areas. For detailed information the reader is referred to Arndt's monograph (*Dermat Ztschr.*, *16* 551 and 645 1909) and to the studies of Trimble and Maloney (*Arch Dermat & Syph.*, 7:452, 1923) and of Michelson (*Arch Dermat & Syph* 7 763 1923)

The *etiology* is obscure The tuberculoid structure of the nodules does not suffice to assume a close relationship to tuberculosis Tuberculoid tissue has been observed in various non tuberculous lesions as for instance, in lichen syphiliticus or in late tuberous syphilomas Tubercle bacilli were never demonstrable in stained tissue sections of lichen nitidus papules one animal inoculation performed by Kyrle proved negative A positive tuberculin reaction noted in a few cases appears not conclusive

Differential diagnosis: The distinction of lichen nitidus from lichen planus may be difficult However the uniformity of the papules in lichen nitidus persists invariably whereas outbreaks of lichen planus usually undergo morphologic changes developing larger polygonal or circular lesions and annular forms. Lichen nitidus retains its skin-colored aspect while the expanding lichen planus lesions present a whitish color or a livid purple hue Most important is the lack of pruritus in lichen nitidus whereas pruritus is usually severe in lichen planus Lichen nitidus must also be differentiated from verruca juvenilis and lichen scrofulosorum However the surface of the former is verrucous and unlike lichen nitidus color is brownish in contrast with the skin-colored papules of lichen nitidus Verrucae juveniles tend to be rather variable in their size and may be linear in distribution. Lichen scrofulosorum occurs primarily in children with active tuberculosis The lesions are scaly and tend to appear in groups

Usually the microscopic picture of lichen nitidus is sufficiently characteristic and there should be little difficulty in identification Recently H. Pinkus and coincidentally other investigators observed Koebner's phenomenon in several cases of lichen nitidus. Pinkus was able to demonstrate the microscopical picture of a characteristic nodule developed on a linear scratching effect showing typical granulomatous infiltrate and loss of basal layer of the epidermis. He concluded that the presence of Koebner's phenomenon can no longer be considered as important in the differentiation between lichen planus and lichen nitidus.

Treatment: As the condition is asymptomatic and relatively inconspicuous, no treatment is necessary Moreover no effective therapy has been reported.

Pemphigus

Pemphigus is a bullous disease of the skin which is generally divided into five types acute pemphigus pemphigus vulgaris pemphigus foliaceus, pemphigus vegetans and pemphigus erythematodes.

In all of these conditions, the anogenital region may be affected. While no attempt is made here to differentiate the various types of pemphigus, still there are certain changes that should be mentioned.



FIGURE 58. Pemphigus vulgaris, vulva. (Moulage, Dermat. Clinic, Univ of Breslau, Prof Dr J Jadassohn.)

In this area, because of friction and moisture, the bullae tend to rupture readily and as a result of secondary changes, both inflammatory and infectious, the lesions may become ulcerated.

Nikolsky's sign is readily demonstrated in these areas.

In pemphigus vegetans, the denuded areas tend to develop hypertrophic granulations, giving this form of the disease its name.

Pemphigus foliaceus may resemble generalized exfoliative dermatitis, but Nikolsky's sign will readily differentiate them

Pemphigus erythematodes with its tendency to form chronic lesions suggestive of pemphigus lupus erythematosus and seborrheic dermatitis does not usually spread to involve the anogenital region but when it does, there is some difficulty in differentiating it from seborrheic dermatitis. In contrast to the involvement of the oral and conjunctival mucous membranes, the genital mucosa is rarely involved in eruptions of pemphigus vulgaris apparently more often in pemphigus foliaceus. However bullae have been noted on the vaginal and vulvar mucosae.

Histopathology: For histologic examination, it is best not to choose a lesion from the anogenital region for study because of the secondary



FIGURE 59 *Pemphigus vulgaris of the genital mucous membranes associated with eruptions of the oral and conjunctival mucosae.* (Dermat Clinic, Frankfurt, Prof Dr O Gans.)



FIGURE 60



FIGURE 61

FIGURE 60 Pemphigus vulgaris of buttocks. The punched out ulcers at the sides of the intergluteal cleft are secondary pressure changes. (Jefferson Medical College Philadelphia.)

FIGURE 61 Pemphigus vegetans. (Univ Clinic, Naples, Prof Dr M Monacelli.)

changes that may be present as a result of trauma, or secondary infection Recent studies by Civatte on pemphigus bullae point to the fact that changes in the epidermal cells are characteristic In his studies, he found the bullae to form usually above a basal layer of the epidermis Because of the loss of intercellular bridges the epidermal cells are not held together and acantholysis results. These epidermal cells show degenerative changes

as well, with a homogeneous appearance of the cytoplasm and swollen nuclei. The basal layer of the epidermis is usually preserved intact. Other investigators such as Winer and Lipschütz are not entirely in agreement with this.

The Tzanck test is a cytologic test based on the presence of these degenerating epidermal cells in the bullae.

Differential diagnosis: Probably the greatest difficulty arises in ex cluding bullous dermatitis herpetiformis from pemphigus. The differentia tion is not made on the basis of the difference in the appearance of the anogenital lesions, but on the basis of the more benign nature of the condition, the less frequent and milder nature of the oral lesions and the microscopic appearance of the bullae.

Diagnostic difficulties may arise in cases where a circumscribed eruption of several bullae appears on the skin of the genitals as an initial manifestation of pemphigus vulgaris. During World War I, we were confronted with such initial eruption consisting of some vesicles and bullae in the genitocrural folds and in the pubic area. In the next several weeks an ex plosive rapid spread of pemphigus revealed the severe fatal disease.

In certain instances of solitary or of several bullae restricted to the genital areas one should not fail to remember that occasionally such lesions may be self inflicted artifacts produced by hysterical individuals or by malingerers.

Therapy: The course of pemphigus has been significantly altered by the use of either adrenocorticotropic hormone or cortisone. Either one can be used with great value and these patients can be kept alive with these substances until remissions occur Much larger doses are required than in the treatment of other dermatoses The medication can then be reduced to a maintenance dose and even completely eliminated until another attack occurs.

The antibiotics are of great value in preventing secondary infection in pemphigus While they do not alter the course of the disease, they are helpful in eliminating or controlling pyogenic infection.

Hailey Hailey Disease

This disease is also known as familial, benign chronic pemphigus and is characterized by recurrent outbreaks of vesicles and bullae in circinate arrangement on apparently normal skin. There is a tendency for early rupture of these lesions with impetiginous crusting

The disease most commonly affects the sides of the neck and axillae but is often seen in the groin.

Histologically this condition presents hyperkeratosis, papillomatosus and similar to pemphigus vulgaris, acantholysis extending to form bullae

many of which are above the basal layer of the epidermis. Dyskeratosis is often pronounced however with the appearance of grains, similar to keratosis follicularis (Darier's Disease)

Treatment: While reports in the literature have suggested that the antibiotics may be valuable in treatment, one of us has treated three cases of the disease which failed to improve with various antibiotics.

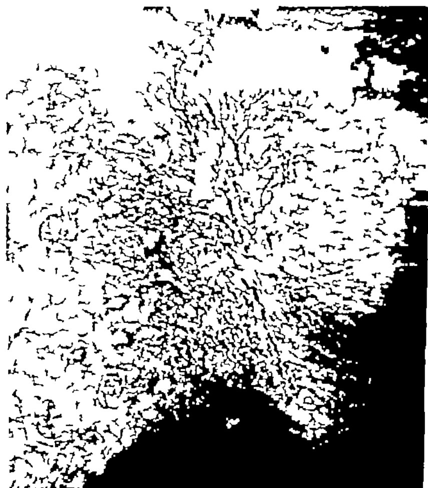


FIGURE 6.—Hailey Hailey Disease of inguinal fold.

PART II

Xanthomatosis

While the anogenital region is not the site of predilection for the various types of xanthoma, these flat or nodular yellowish lesions vary in *size from a few millimeters* to a centimeter in diameter and develop very

slowly They may be present on the skin of the penis scrotum or the labia and are even more rarely seen in the vaginal mucosa.

Histologically the large foam cells are diagnostic.

In *xanthoma tuberosum*, the distribution of the pinpoint to cherry stone sized nodules over the extensor surfaces of the joints, scattered irregularly over the trunk and on the palms and soles helps to differentiate this form of xanthomatosis The blood cholesterol is usually increased, but the total blood lipids are usually normal. It is well to keep in mind that many of these individuals have similar infiltration of the coronary arteries.

Tuberous xanthomatosis has been described as a familial or hereditary condition with dominant inheritance. Recently Leys reported its occurrence in three generations of a family with a fatal coronary involvement in the



FIGURE 63. Xanthoma tuberosum multiplex. (Univ Clinic, Breslau, Prof Dr J Jadassohn.)

oldest child of twelve years, and with arterial claudication and Stokes-Adam s syndrome in the second child of the third generation.

Figure 63 shows xanthoma tuberosum of the scrotum, the yellowish nodules being closely aggregated on the scrotal skin and spread over areas of the penis and the inner surface of the thighs.

In xanthoma disseminatum, the lesions are seen on the flexor surfaces of the extremities, especially the axillae. Xanthelasma is commonly present and the fine papules of the disease tend to involve also the face and the mucous membranes. The blood lipids are within normal limits The disease does not tend to involve the coronary arteries.

Involvement of the genital region also occurs in xanthoma dia beticorum In these patients diabetes is present and the blood lipids are increased.

Treatment In xanthoma tuberosum, a low fat diet may cause a resolution of the nodules. In xanthoma diabeticorum proper management of the diabetes and of the blood lipids will often cause the nodules to shrink.

If the nodules are quite large and cause discomfort to the patient, they can be surgically excised. It is well to keep in mind the serious nature of xanthoma tuberosum when lesions involve the coronary arteries and these patients should be carefully examined and observed in regard to their cardiovascular status

Scleroderma

Very rarely the genitals are the site of a solitary plaque of scleroderma. Scherber described such incidence. A single distinctly bordered lesion was found on the distal part of the prepuce extending somewhat to the inner sheath of the prepuse. The yellowish white plaque was surrounded by a



FIGURE 64. Scleroderma. Not contraction of skin above mons pubis and thinning of pubic hair

small reddened inflammatory area. The histologic picture confirmed the diagnosis

More frequently the anogenital region is included in general eruptions of scleroderma. Scleroderma of the abdominal skin or the groins may extend to the skin of the penis and scrotum forming characteristic plaques often associated with pigmentary changes "Sclérodermie en plaques" as well as "sclérodermie en bandes" have been described on the dorsal skin of the penis

Figure 64 shows scleroderma of the pubic region in a female Note contraction of the skin above the mons pubis, and thinning of pubic hair

Lichen Sclerosus et Atrophicans

Lichen sclerosus et atrophicans of the anogenital region and its particular importance in the modern etiopathogenesis of sclerotic atrophic dermatoses of the penis will be discussed in Chapter 14

Chiefly based upon similarities of the histologic picture, a possible relationship between lichen sclerosus et atrophicans and kraurosis vulvae has been suggested by various authors (C. A. Hoffmann, 1914 recently Laymon, C. Chapter 14) C. A. Hoffmann described two cases of lichen sclerosus et atrophicans of the vulva, the one associated with cutaneous eruptions and those of the oral and lingual mucosa, while in the second case the eruption was limited to the vulva (fifty year-old woman showing bilateral lesions of the labia majora and typical eruptions on the contact surfaces of the thighs pinpoint to pinhead sized sharply circumscribed, disseminated or confluating, nonelevated lesions were found on pigmented areas with atrophy in various lesions)

Fox Fordyce Disease

Fox Fordyce Disease a chronic itching dermatosis consisting of discrete small, pinhead to small pea sized, densely grouped papules of normal skin color or showing a slightly red to brownish hue, is found predominantly in the female. Although rare this condition must be included in our description for practical and especially for diagnostic reasons It is located more frequently in the axillary region, often in the pubic area, and rarely around the umbilicus or the nipples. It is a most annoying disease due to persistent intense itching, often causing sleeplessness.

The *etiology* is still under discussion While some investigators consider Fox Fordyce to be a variant of circumscribed neurodermatitis, the opinion seems to prevail that it is caused by dysfunction of the apocrine glands, leading to irritation by the excreted sweat.

Histology: Acanthosis and parakeratosis around the ducts of the glands and degenerative changes of the lining cells of the coils. Lymphocytic infiltration and accumulation of cellular elements of the connective tissue in the corium are found.

The *differential diagnosis* includes lichenoid eruptions of neurodermatitis and lichen planus. However the limitation to the axillae or/and pubic regions and the extremely annoying itching are significant of Fox Fordyce disease Lichen planus would rarely be seen restricted to the location of the latter disease.

The *treatment* of Fox-Fordyce disease presents a difficult problem The condition is most resistant to local treatment. Pruritus does not satisfactorily respond to the usual remedies. Favorable results of Roentgen irradiation proved to be transitory

Lupus Erythematosus

Rare though it is, the occasional occurrence of chronic discoid lupus erythematosus in the anogenital region must be considered in the differ

The reader is referred to O Gans *The Skin Picture in Hematopoietic Diseases* (*Arch Dermat & Syph* 16 1 1927) to F Pinkus (*Arch Dermat u Syph* 50 37/177 1899) and to O Gates (*Arch Dermat & Syph.,* 37 1015 1938)

The *differential diagnosis* of leukemic tumors does hardly offer diagnostic problems when connected with facial leontiasis or tumors elsewhere on the body Spontaneous regression is very rare. Leukemic tumors of the genital or pubic regions must be differentiated from mycosis fungoides. In the majority of cases the basic blood disease will have been revealed long before the full development of each tumor

Cutaneous reactions to myelogenous leukemia are rare (pustules, urticaria, pruriginous affections) These reactions are considered as nonspecific exceptionally nodules or tumors of brownish-red color may be seen resembling those occurring in lymphatic leukemia.

Treatment depends thoroughly on careful examination of the blood revealing the definitive type of leukemia, the examination of the inner organs and the possible involvement of the lymphatic glands. In addition *pruritic conditions may support the diagnosis Roentgen therapy plays an* important role in the treatment of skin tumors in leukemic disease. The treatment of leukemic diseases is thoroughly discussed in textbooks of internal medicine and pediatrics

Pseudolues Papulosa of the Female Genitals

Pseudolues papulosa of the female genitals first described by Lipschutz, in 1921 under this non-committal term is a rare but diagnostically important non venereal affection The origin as well as the definition of this condition as a possible disease entity are still under discussion

Lipschutz s clinical and historical description has remained valid up to the present time The condition is found in adolescent and adult females, very rarely in children. The age incidence in Lipschütz series of cases ranged from fifteen to thirty-five years A. Alexander described a case in a girl of twelve years of age, who had been raped shortly before examination. Variants of the classical type described by Lipschutz, have been demonstrated in infants presenting papular pustular and ecthymatous lesions at the same time A. Alexander doubted the validity of these reports. He inclined to classify those eruptions as variants of the "*dermites infantiles simples*" of the French authors, with special reference to Jacquet s syphiloide postérosif

The rather firm distinct, roundish or hemispheric, lenticular to pea sized papules and button like formations resemble very closely syphilitic condylomata. The lesions appear on otherwise normal skin areas and are usually located on the labia majora, less frequently on the perianal skin.

The color of the surrounding skin is likewise normal, while that of the lesions appear more grayish white As in syphilitic condylomata, there is no pain or itching and only a slight tendency to ooze. The inguinal glands were never involved. Serologic tests and dark field examinations for spirochaeta pallida always yielded negative results.



Figure 65 Pseudolues papulosa, Lipschütz, versus Jacquet syphiloide postérosive, in an eight month old infant.

Later reports by Planner Höcker Gay Prieto and E. Hofmann confirmed Lipschütz findings. In most cases the lesions disappeared spontaneously under the hygienic conditions of hospitalization after about eight days. There were no scars or residual pigmentation. In contrast to these reports, Alexander reported considerable resistance to therapy in his patient.

Histologic findings revealed merely uncharacteristic inflammatory changes associated with acanthosis and parakeratosis. The infiltrations

usually showed few or no plasma cells The histological picture is therefore easily distinguished from that of syphilitic papules

The *differential diagnosis* from condylomata lata is very important. In certain instances pseudolues papulosa must be distinguished from Jacquet's "*érythème syphiloïde postérosif*" a well-defined, but etiologically unexplained affection Lesions of pseudolues papulosa in infants may closely resemble the papular stage of Jacquet's disease. Alexander has emphasized, however that this stage of dermite papuleuse is seldom encountered without simultaneous manifestations of the erythematous stage Lichen obtusus (Unna) may resemble the lesions of pseudolues papulosa, but is histologically definitely different presenting all the characteristics of lichen planus

Therapy: As described above cleanliness and elimination of exogenous irritation seem to suffice to stimulate spontaneous healing Under the conditions of ambulatory treatment, the lesions show less tendency to regression and require auxiliary local therapy with mild lotions or dusting powders (salicylic or boric acid powder)

Figure 65 is presented to demonstrate the difficulties when differentiating Lipschütz pseudolues papulosa from Jacquet's syphiloide postérosif While the button like firm lesions in the margins of the labia majora correspond to the lesions characteristic of Lipschütz disease the pustular eruptions of the surrounding region correspond thoroughly to the multiform lesions occuring in Jacquet's disease. Our observation refers to an eight month-old infant repeated darkfield examination and serologic tests on syphilis negative. Healing within two weeks under local treatment with neomycin ointment

Acanthosis Nigricans

This is a rare benign dermatosis found in children and adults, presenting in the folds of the body hyperpigmentation and papillomatous growths. It frequently involves the pubic and inguinal regions and the external genitalia. Cases seem equally divided between a so-called malignant type and a benign type The malignant type is associated with internal adenocarcinoma.

According to H. O Curth, the benign type usually begins in childhood or at puberty and gradually spreads and finally becomes arrested or regresses Familial tendencies have been noted.

In malignant acanthosis nigricans most cases begin in middle or old age and the eruption has become widespread by the time the adenocarcinoma is noted. No familial tendencies have been recorded. The adenocarcinomata accompanying this condition is invariably highly malignant.

Curth believes that acanthosis nigricans and cancer may have a common cause which is of a genetic nature.

Pseudo-acanthosis nigricans occurs in obese brunet individuals with usually less pronounced changes. It tends to disappear with loss of weight.

Histologically the disease shows hyperkeratosis pronounced acanthosis, with atrophy of the prickle cell layer increased pigment in the basal cell layer and upper corium. The cutis shows slight perivascular lymphocytic infiltration.

Treatment: The presence of malignancy in acanthosis nigricans should alert one to the immediate need for thorough study of the patient, to locate and treat the adenocarcinoma. There may be temporary regression of the cutaneous lesions after treatment of the malignancy Local treatment is ineffective.

Cornu Cutaneum

Cornu cutaneum is the term used to designate horn-like excrescences chiefly located on the scalp face the hands and fingers, and occasionally on the skin of the genitals. Cornua cutanea have been described as



FIGURE 66. Cutaneous horn. *J Urol.* 52 611, 1944. Courtesy of Dr J A. Taylor

grotesque horny formations on the glans penis and prepuce (case Taylor Fig. 66)

These neoplasms may develop in an area of normal skin morphologically identical excrescences however are encountered at the sites of pre-existing lesions. Cornua cutanea slowly develop upon scars of varied origin (trauma, burns lupus vulgaris) nevi, warts senile keratoses and



FIGURE 67a Same patient histological picture L. P (Taylor)

epitheliomas. They may persist unchanged for an indefinite time or may grow slowly to form conical, cylindrical or tortuous malformations. Among eighty three cases of cornu cutaneum, D W Montgomery recorded twelve instances combined with, or based upon epitheliomas.

Histology: The true cornu cutaneum consists of a stratified mass of hyperkeratotic and parakeratotic lamellae and columns with or without some nuclear residues. Occasionally the papillary bodies may show some



FIGURE 67b. Same patient, magnif. × 1400 (Taylor)

lymphocytic cell infiltration and plasma cells probably as a result of external irritation of the horn. The histologic appearance of the underlying tissue varies according to the origin of the neoplasm. Its pathogenesis remains problematic, because the same structure appear upon normal skin as upon pre-existing skin alterations.

Treatment: Only radical extirpation or destruction including the under lying tissue will prevent local recurrence The tissue should always be examined microscopically because of the possibility of malignant changes.



FIGURE 67a. Same patient, histological picture L. P (Taylor)

epitheliomas. They may persist unchanged for an indefinite time or may grow slowly to form conical, cylindrical or tortuous malformations. Among eighty three cases of cornu cutaneum, D W Montgomery recorded twelve instances combined with, or based upon epitheliomas

Histology: The true cornu cutaneum consists of a stratified mass of hyperkeratotic and parakeratotic lamellae and columns with or without some nuclear residues Occasionally the papillary bodies may show some

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Leucoderma refers to depigmentation secondary to inflammatory reactions in the skin. Leucoderma syphiliticum, usually located in the neck, has been found also in the genital region (Ehrmann 60 per cent on the neck, 20 per cent on the genitals in syphilitic women 3 per cent on the genital region in syphilitic men) Also leucoderma psoriaticum has been observed in this location. Downing reported leucoderma of the glans penis as a result of exposure to rubber condoms.

Congenital Pigment Accumulations

The various forms of nevi encountered in the genital region will be discussed in Chapter 15.

A typical example of a pigmentation of phylogenetic origin is the *mongolian spot*" of the sacral region. It is found in 90 to 98 per cent of all infants of Mongolian, Chinese Japanese and Negro ancestry Appearing soon after birth, it fades away within the first few years of life. Japanese investigators observed such spots as early as during the fifth to six month of fetal life (Ishikawa) Exceptionally the pigmentation may persist up to the tenth or twelfth year The color is blue or grayish blue in Mongolian descendants and grayish green in those of Negro descent. Occasionally mongolian spots occur in infants of white ancestry

Histologically the Mongolian cells are found chiefly in the deeper layers of the corium, they are filled with fine melanin particles. The cells are of irregular or spindle shape, never accumulate in lumps and never show the dendritic processes of melanoblasts (O Gans)

Meirowsky and Leven explained the Mongolian spot as a remnant from our animal predecessors. There are similar pigmentations in the animal realm as, for instance, the deep corium pigmentations in the sacral region of monkeys.

The Mongolian spot is located almost exclusively in the *sacral* area. Recent authors, however have described *extrasacral* spots as "persistent aberrant Mongolian spots found on the extremities, the face, the eyelids and on the bulbar conjunctivae. The number shape, and size of these extrasacral spots varied considerably (Reese- Cole and associates)

Differential diagnosis: Mongolian spots in white subjects must be distinguished from certain forms of nevi. Their spontaneous disappearance within the first two or three years contrasts with the permanent character of true neviform anomalies. The above mentioned *aberrant* Mongolian spots should not be confounded with the rare "*blue nevus* described by Tièche (1907) Blue nevi are found chiefly on the face and the dorsum of the hands or the extensor surfaces of the extremities. The tinge of the Tièche nevus is said to be darker than that of the Mongolian spot, and, significantly the blue nevus presents a slight infiltration to the palpating

finger Differentiation of the two anomalies may prove difficult however when the aberrant Mongolian spots are not associated with a spot in the typical sacral region Histologically the pigment cells of the blue nevus are most similar to Mongolian cells and like the latter are found chiefly in the lower part of the corium. A close relationship or even a possible identity of this variant of the Mongolian spot with the blue nevus has been suggested (Pariser and Beerman) However that may be, the term aberrant Mongolian spot should be reserved for extrasacral Mongolian spots combined with sacral spots.

Vitiligo

The anogenital region is one of the most common starting points of *acquired leukopathia or vitiligo* In this condition there is simultaneous depigmentation and hyperpigmentation The milk white round and oval spots



FIGURE 68 Vitiligo.

varying in size from that of a dime to a palm, show a marked increase of pigment formation around their convex outlines. The contrast is most obvious in Negroes A similar contrast is observed also in vitiligo spots that have been exposed to sunlight or to therapeutic irradiations, and may become exaggerated in the genital region during pregnancy A tendency to symmetrical distribution is noted in vitiligo of the genital region A bilateral symmetrical development in the inguinocrural folds is frequently observed. Unilateral vitiligo of the genitals is very rare.

The first manifestation of genital vitiligo may remain unnoticed for

a long time. The patient in Figure 68 was not aware of the widely spread white spots before ramifications of perineal and scrotal depigmentation areas encroached on the skin of the inguinal region and the thighs. The hair in the involved areas is usually included in the process of depigmentation. The mucous membranes are rarely affected in vitiligo Some instances of vitiligo of the labia minora have been reported and a few cases in which the vitiligo extended to the inner sheath of the prepuce and the glans in Negroes (Atkinson, cited by Habermann)

The development and course of vitiligo are very slow After having reached a certain extent, the condition may remain unchanged for years. However a more rapid progression is occasionally observed.



FIGURE 69 Leucoderma penis.

Histology: Except for the absence of pigment, the vitiligo spot is not associated with any pathologic symptoms Occasional findings of inflammatory changes if marked, are usually due to exposure to therapeutic irradiations. The area surrounding a vitiligo spot shows considerable accumulation of pigment cells.

Etiology: The origin of vitiligo is still unknown All interpretations available are hypothetical. The condition has been ascribed chiefly to endocrine or trophoneurotic disturbances and to toxic influences.

Differential diagnosis: The configuration of the white areas in vitiligo, their convex outlines, their hyperpigmented borders, and slow course almost exclude any diagnostic difficulties. In partial albinism, there is no increased pigment formation in the marginal zone, the distribution is more irregular and the congenital and hereditary character excludes acquired leukopathia.

Therapy: Recent investigations by El Mofty and others suggest that some patients with vitiligo may respond to treatment with ammidin Location of vitiligo in the anogenital region does not present a cosmetic problem and therefore, can be ignored. Ammidin is a purified compound, prepared from the plant Ammi majus, Lynn

Pigmentary residue of dermatoses of the anogenital region, their most diversified origin has been previously explained. No definite diagnostic

conclusion can be drawn from the presence of residual pigmentation in the absence of additional symptoms elsewhere on the body In certain cases however the shape grouping and dissemination of the pigmentary spots, and, in addition, the patient s history may suggest their origin. The nuance of color may also have suggestive significance. However it must be kept in mind that the tinge may vary in individual cases according to the depth and density of the pigment accumulation

The significance of the so-called taches bleues persisting after phthiriasis is discussed in Chapter 3

A careful general examination is imperative especially in cases of *diffuse* hyperpigmentation The reader is referred to the introduction of this chapter Pregnancy diseases of metabolism nutritional deficiencies abdominal cancer and dysfunction of the adrenals, the pituitary and thyroid glands must be taken into consideration. In the presence of annular or serpiginous pigmentations, with or without scar formation it is most important to make a thorough inquiry for a possible preceding syphilitic process. More or less extensive perianal and perivulvar pigmentations associated with atrophy telangiectasis and scarification or ulceration are characteristic sequelae of previous Roentgen damage.

Changes of the Pubic and Genital Hair

Every hyperpigmentation and depigmentation in the genital region may involve the hair of the affected areas. This refers to both acquired and congenital pigmentary changes.

Hyperpigmentation is common in the hair of moles. Hypertrichosis is most marked in pigmented nevi especially in the *swimming trunk nevi* covering the genital and lumbosacral region Localized hypertrichosis without an underlying nevus formation is often found in the *sacral* region. Hypertrichosis occurs on an hereditary basis but also as an acquired phenomenon due to endocrine conditions (pituitary tumors hypo- or hyper thyroid states)

Loss of pigment is seen in congenital hypotrichosis and in partial albinism of the genital region as likewise in nevi depigmentosi. Piebaldism in the Negro may be apparent in the hair of the genital region. Loss of pigment in the hair on vitiligo spots has been previously mentioned.

Like the hair of the scalp so also the pubic and genital hair are subject to the physiologic process of *decoloration* with advancing years. Premature grayness including this region is significant of Simmond s disease (hypophyseal cachexia) Thinning, decoloration and loss of the axillary and pubic hair likewise occur in this disease.

The hair of the genital region may be involved in all forms of alopecia, i.e. in alopecia areata as well as in the severe form of alopecia totalis,

which involves the entire body and in its excessive form, also the lanugo hair

Partial or total loss of the pubic and genital hair is seen also as a sequela of localized dermatoses resulting in atrophy or cicatrization (scleroderma, Fox Fordyce disease of the pubic region, deep mycotic infections, etc.)

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ditional administration of vitamin B compounds. In mild cases relief was evident after twenty four to thirty six hours. More severe cases demanded a prolonged treatment with consideration of all factors responsible for deficient absorption of nutrients from the intestine and for other organic



FIGURE 70 Genital and anal changes due to avitaminosis (ariboflavinosis) (Dermat. Clinic, Frankfurt, Prof Dr O Gans.)

dysfunctions. Local treatment is of minor importance unless secondary infection requires special attention.

Pellagra

The etiology of pellagra is still under discussion. It is generally agreed that a prolonged faulty diet and an insufficient utilization of foodstuffs play an essential role. *A diet devoid of proteins minerals and vitamins and* especially of nicotinic acid, obviously predisposes the subject to pellagrous eruptions.

For a long time the assumption prevailed that pellagrous eruptions develop only on the uncovered parts of the body which are exposed to the sunlight. This theory could not be upheld, however after unquestionable pellagrous eruptions were observed in covered regions of the skin such as the armpits the covered parts of the upper arms and thighs, and on the feet. This finding does not exclude an activating influence of sunlight in precipitating eruptions of pellagra in the spring.

The involvement of the anogenital region in pellagra is certainly unusual, but, as Merk stated, it may be observed more frequently if this area is inspected in every case of pellagra. Merk described and illustrated a pellagrous erythema of the scrotal skin (see references) Other reports in the literature appeared inconclusive.

The reaction of the genital region to *vitamin C deficiency* may lead to lesions of the vulva and vagina similar to those seen in this disease on the oral mucosa, the tonsils and pharynx. The specific dietary factor in vitamin C deficiency is ascorbic acid the antiscorbutic vitamin. The hemorrhagic ulcers of the mucous membranes resulting from brawny or solid blood extravasates, fall an easy prey to secondary infection with streptococci, bacilli of the diphtheria group or fusospirochetosis. Of very rare incidence as compared with tonsillar or pharyngeal lesions submucosal hemorrhages of the vaginal mucosa may easily be overlooked. Prior to breaking down, they appear merely as more or less indistinct pain less swellings usually associated, however with petechiae and ecchymoses of the genital region and other parts of the skin surface.

Differential diagnosis: In the presence of other symptoms characteristic of scurvy the diagnosis will suggest itself by swelling of the gums, oral hemorrhagic lesions, painful joints, roentgenographic changes in the bones, anemia. In obscure cases, the differential diagnosis must include the blood dyscrasias, in particular agranulocytosis. Clinically ulcers of the mucous membranes associated with diseases of the hematopoietic system, are hardly distinguishable from those in scurvy However besides the patient's history a careful blood analysis will reveal a marked reduction in the number of granulocytic cells or of leukopenia in the blood. Multiple ulcers of the posterior wall of the vagina due to *agranulocytosis* have been described by Otto (see Chapter 12)

Therapy: Besides the dietary treatment of vitamin C deficiency in scurvy in the presence of hemorrhagic necrotic ulcers of the mucous membranes also the administration of penicillin or aureomycin is indicated to prevent septic infection Local treatment with solutions of hydrogen peroxide (rinsing and dressings according to location) are recommended to prevent the regression of ulcers of the vulva or vagina. Dietotherapy may be supported by the additional administration of vitamin C com pounds.

The manifestations of *vitamin A deficiency* are of minor significance in the scope of our description Vitamin A and its precursor carotene, are dietary constituents important for maintenance of the epithelial structure of the skin the mucous membranes and especially the retina. The skin symptoms of this deficiency disease when involving the genital region are always those of the skin in general, with dryness and roughness associ-

ated with the development of small spinous papules in the vicinity of the hair follicles. The lower abdomen the buttocks, the anterolateral aspect of the thighs constitute sites of predilection Eye symptoms are of supreme importance Night blindness may precede and keratomalacia may follow the cutaneous manifestations in serious cases. The recently suggested, as yet hypothetical etiological role of Vitamin A deficiency in leukoplakia vulvae has been discussed in Chapter 14

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CHAPTER 11

GENERAL PRINCIPLES OF TREATMENT

The peculiar anatomical and functional variations of the anogenital region make it necessary to exert care in the choice of therapeutic measures in the management of conditions affecting these areas No attempt is made here to present a complete formulary for dermatologic therapy We are con cerned chiefly with supplementing the therapeutic measures described in previous chapters and at the same time, to outline the general principles of treatment of the affections located in this region of the body

External Treatment

The importance of an appropriate external treatment cannot be over emphasized in the management of diseases involving the anogenital region. Cleansing measures are of great importance in avoidance of local irritation. The use of wet dressings, powders, lotions emulsions, pastes and ointments has its own individual indications in the treatment of conditions affecting these areas Physical agents such as the local application of acids or Podophyllin have important uses especially in these areas.

Measures of Cleansing

In the management of most diseases involving the anogenital region, proper cleansing is important in eliminating irritation but soap and water should be avoided. Tub baths may be used, taking advantage of the non irritating qualities of starch, oatmeal and sodium bicarbonate. Local sponging with starch water normal saline or boric acid solution should be done gently so as not to add further irritation of friction to the already sensitive areas.

Cleansing after a bowel movement is necessary and it is best to avoid the local use of *toilet paper in favor of cotton moistened with any of the* above solutions and applied gently

Local Therapy

The principles of local therapy as directed to the anogenital region, are in general those that are followed out in the treatment of all cutaneous conditions but they do vary not only according to the stage of inflammatory

reaction, i.e., acute subacute or chronic, but also because of the peculiar features of the area.

Acute stages of an eczematous dermatitis should be managed with mild soothing applications Wet compresses are most effective It is recommended that they be made of surgical gauze from twelve to fifteen layers thick and kept moist for the entire time that they are placed against the inflamed surface They should be of room temperature or cooler in order to aid in vasoconstriction and the solution placed in a convenient location, so that the patient may readily remove the compress dip it in the solution, wring it out and reapply it. Because of the location it is usually necessary for the patient to be lying down for proper application Typical solutions to be applied with these compresses are saturated solution of boric acid, Burow s solution and normal saline solution

It should be emphasized that these wet compresses are most effectively used in the *acute* stage of an eczematous dermatitis, which is characterized by the presence of redness, edema, vesiculation oozing and crusting Such an acute stage of inflammatory reaction is more or less incapacitating to the patient and therefore, the enforced rest necessary for the application of such compresses is indicated

Shake lotions are also of value at this stage These consists of watery suspensions of a powder which is then deposited on the skin. Vasoconstriction and counterirritation occur with evaporation of the watery base of the lotion and the dry powder remains on the skin for its soothing effect on the acute inflammation. Such lotions are conveniently applied and do not require immobilization of the patient For this reason, they are of great value when the patient s disease is not severe enough to require the use of compresses, but there is still the acute stage of an eczematous dermatitis present

In some instances the compresses can be applied for approximately a half hour twice daily and the lotions used the remainder of the time Typical examples of such lotions would be suspensions of zinc oxide in water such as calamine lotion, N F

The *subacute stage* of an eczematous dermatitis shows less inflammation and therefore less erythema and edema Because there is less edema there is absence of vesiculation oozing and crusting The skin is dry and scaly in this stage

Wet compresses are of less value here than in the acute stage and tend to increase dryness except when restricted to short periods of application. Lotions also may be used during this stage but, here again one should guard against allowing the skin to become too dry as fissuring may occur in the inguinal folds, beneath the prepuce over the scrotum and in the intergluteal cleft.

Emulsions are frequently of value in the subacute stage of an eczematous dermatitis and the following prescription may be useful

Sodium borate		4.
Olive oil		
Liquor calcis	āā q.s.	180
Span q.s to emulsify		

This may be applied q.i.d.

At this stage, pastes are also valuable adjuncts to therapy and the following formula may be helpful in less acute phases of the subacute stage

Zinc oxide		
Starch	āā	2.
Petrolatum	q.s	30

At this stage of the dermatitis the patient should be observed carefully and if flares occur causing a regression to the acute stage of the dermatitis the treatment should be changed as promptly as possible for greatest relief and compresses and/or lotions applied

The *chronic stage* of an eczematous dermatitis shows lichenification, i.e., thickness dryness and scaling of the skin with an accentuation of the normal folds Lichenification is less apt to be noted on the glans penis, *prepuce and the thin skin of the perianal region, just adjacent to the anal* ring At this stage, greasy ointments are usually well tolerated, as they help to combat the discomfort of dryness accompanying this stage and therefore, fissuring of the affected areas is more readily controlled.

However one should keep in mind, at the same time, that excess usage of greasy ointments may cause a secondary grease folliculitis that can be difficult to control because of moisture and friction in these areas.

It is well to remember that regardless of the activity of the ingredients (antibiotics, sulfur mercury etc.) used in the treatment of these stages of an eczematous dermatitis, these general principles should be kept in mind. Otherwise some difficulties of secondary treatment irritation may arise as a result of the effects of the bases alone, entirely apart from the active chemicals contained.

While crude coal tar and its derivatives are useful in the chronic stage of an eczematous dermatitis affecting other areas, it is necessary here to be careful regarding the development of a tar folliculitis in the anogenital region

Antibiotics

The antibiotics have undoubtedly influenced the management of py ogenic infections of the skin. Some of these diseases such as carbuncle and

erysipelas have undergone a tremendous reduction in incidence. Other pyogenic diseases show more rapid response to treatment.

In general they can be divided into two groups. Group 1 the bactericidal antibiotics are penicillin, streptomycin tyrothricin, bacitracin polymyxin B and neomycin The Group 2, bacteriostatic antibiotics are chlortetracycline oxytetracycline, tetracycline and chloramphenicol. Recent work by Jawetz and his co-workers seems to show that a synergistic action exists when two antibiotics of either Group 1 or Group 2 are mixed. Antagonism often occurs if a member of the bactericidal group is combined with one of the bacteriostatic antibiotics. However this synergism and antagonism does not always occur and cannot be predicted. According to Klein and Schorr it depends in great part on the susceptibility or resistance of the organisms

As with the sulfonamides, it was found early that it was inadvisable to administer penicillin topically because of the development of hypersensitivity Such hypersensitivity excludes the possibility of using this valuable antibiotic parenterally However bacitracin polymyxin B and neomycin are of limited or no value parenterally and are valuable topical antibiotics Polymyxin B seems especially valuable in infections caused by the bacillus pyocyaneus. The bacteriostatic antibiotics in Group 2, chlortetracycline, oxytetracycline tetracycline and chloramphenicol are used orally but the latter has fallen into disfavor because of fatal toxic reactions. All of the Group 2 antibiotics may produce nausea, vomiting, proctitis and diarrhea.

Sulzberger and Baer have most aptly pointed out that because of the ready accessibility of cutaneous infections the antibiotics have not entirely replaced previous forms of external medication and, therefore, such measures should not be discarded in many instances. While sensitization reactions are not as frequent with the topical use of the antibiotics as with the sulfanomides, yet penicillin and streptomycin should be used with caution, if at all. The other antibiotics appear to have a very low index of sensitivity

Livingood and others believe topical neomycin, in ointment form to be the most desirable antibiotic. It has a low sensitizing index, is colorless, stable and is not used systemically

Because of its stability neomycin can be used in lotion form with 6 mg in 120 cc. of a simple zinc oxide lotion. This is especially valuable in the anogenital region because of intertriginous changes from moisture and friction. The use of a lotion is also valuable in the pubic region to avoid the development of grease folliculitis which can readily develop from the use of an ointment in this area.

The use of the antibiotic sensitization test seems of greatest value in the management of chronic pyogenic diseases such as hidroadenitis suppurativa.

In the more superficial pyogenic infections, such as impetigo the disease has not infrequently been cured before the studies have been completed.

Great care of course, should be taken when these studies are performed, to have as pure a culture as possible from an unruptured abscess. In infections such as hidroadenitis suppurative, most of the oral antibiotics can be tolerated well over a period of months.

Radiation Therapy

X ray and radium can be of value in the treatment of cutaneous diseases of the anogenital region. However radiation therapy should be used with caution, both because of the chronicity of many of these lesions and the tendency for repeated dosages to be given and also the presence of highly radio-sensitive tissue (the testicles) in this area.

It is suggested that the testicles be pushed up into the inguinal canals and held there by the hands during treatment of lesions of the scrotum. The hands should be covered with lead foil for protection. MacKee and Cipollaro are of the opinion that four to six weekly treatments of 75 Roentgen units of superficial unfiltered x ray can be given to this area without danger but if further treatment is needed, the semen should be examined every few weeks and it may be well to have the written permission of the patient to proceed with his treatment. One usually finds however that if there is not improvement with four to six weekly treatments, it is unlikely that further radiation therapy will further influence the condition.

There seems to be less danger of injury with the use of the soft beta rays of radium in this area. For this purpose, a half strength radium applicator screened with rubber tissue or oiled silk is effective With this method, the effect of the radiation can be more easily obtained because of the curving contours of the anogenital region and weekly treatments given for one to two minutes are very helpful.

Grenz rays appear to be less damaging, but until much more is known with extensive medical application of this medium it is well to be careful here, also.

Thorium-X and radon may also serve some useful purposes in the treatment of radio-sensitive superficial cutaneous lesions affecting this area. Collodion and alcoholic solutions give better control of application than ointments in these areas.

Electrosurgery for both cutting and coagulation bears special warnings in its use in these areas.

ACTH and Cortisone

The use of adrenocorticotropic hormone and cortisone have been definite advances in the management of many dermatologic conditions. They

have been life-saving in many cases of pemphigus and have appeared to temporarily improve severe exacerbations of acute disseminated lupus erythematosus. However their greatest value appears to be in the management of self limited diseases producing severe incapacitating symptoms. This is especially noticeable in cases of acute contact dermatitis where the cause can be promptly removed and the symptoms rapidly disbursed through the use of these substances. No attempt can be made here to completely outline the methods of use, but certainly warnings regarding serious side effects should be emphasized.

The use of hydrocortisone in ointment form, for the relief of itching, and the improvement of eczematous processes, is important. It should be pointed out that the thin skin of the anogenital region lends itself readily to absorption of this medication from topical applications and therefore it can be very valuable in the management of itching and eczematous eruptions affecting this area. The 1 per cent strength of hydrocortisone ointment seems satisfactory and should be applied three or four times daily.

These substances when administered parenterally should be used with caution in the management of those diseases which are not self limited. This is especially important in neurodermatitis where the patient tends to depend on the medication for improvement and neglect other more important measures which would be of more lasting effect in preventing recurrences.

Psychotherapy

In these days of aroused interest in psychosomatic medicine it has been well said that no general practitioner or specialist can afford to be without some elementary understanding of psychotherapeutic procedure. The physician fully aware of the important and often determining role of emotional shocks, frustrations, worry, fright and sexual problems in the pathogenesis and persistence of the conditions under discussion, must cultivate a sympathetic and tactful approach in an effort to gain the confidence of his patient. Frequently the mere telling of his difficulty may have the effect of a psychocatharsis and prove beneficial. It is furthermore important that the patient himself should be instructed concerning the possible influence of such factors in order that he may be able to cooperate more fully with the physician. In this psychotherapeutic approach, the physician must limit himself to very simple measures, and in any case where a real psychosis is suspected, should at once refer the patient to a psychiatrist.

Mental and physical rest as well as sedative treatment are helpful adjuncts. Occasionally removal from the family, a short vacation or other interruptions in the daily routine of life may prove beneficial.

Many treatments are psychogenic in effect, even though not intended as such. Frequently the condition may disappear spontaneously or respond to placebo therapy Patients who have been apparently cured, may suffer relapses following emotional shocks or periods of intensive anxiety Another matter that requires consideration in selecting therapeutic measures is the fact that some of these treatments may have the effect of creating a fixation complex.

Addendum

At this time there are some additions to be made in treatment of nonvenereal diseases of the anogenital region

9-Alpha Fluorohydrocortisone Acetate in .1 and .2 per cent ointments have proven to be of value in the treatment of eczematous conditions. This substance itself is unquestionably more potent than Hydrocortisone Acetate or free-alcohol and ointments of these strengths have been satisfactory when used instead of the Hydrocortisone preparations. We have noted that an occasional patient with itching of the anal region has responded to 0.1 per cent Fluorohydrocortisone Acetate ointment, even though there had been no previous improvement with ointments containing as high as 2½ per cent Hydrocortisone Acetate.

The so-called tranquillizing medications can be of value in the general management of patients with itching and psychogenic factors. Chlorpromazine Hydrochloride (10-(3-Dimethylaminopropyl) 2-Chlorphenothiazine Hydrochloride) 10 mg. t.i.d. and Reserpine .25 mg q.i.d. have been very valuable in many instances in relieving nervous tension. Chlorpromazine (Thorazine) seems to be more rapid in its action whereas Reserpine requires from ten to fourteen days for its full effect to become manifest.

These preparations are helpful in the management of some cases of neurodermatitis.

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PART II

THE "NONVENEREAL ULCER" OF THE GENITALS

A. Introduction
B Ulcerations Due to Mechanical, Thermal, Chemical and Physical Trauma
C. Ulcerations Caused by Other Infections Than Venereal Disease
D Ulcerations of the Genitals in Acute Infectious Diseases
E. The Malignant Genital Ulcer
References

A. Introduction

Experience has proven that numerous patients of both sexes take no notice of inconspicuous lesions of the genitals until ulceration and/or pain give rise to a visit to the physician. The presence of a small uncharacteristic ulcer may then confront the physician with diagnostic difficulties unless the results of dark field examination or the history suggest the presence of a venereal disease.

The diagnosis of an atypical genital ulcer will be more difficult in the presence of a *chronic* ulceration previously subjected to local treatment.

Progress of etiological research and modern diagnostic methods have obviously reduced the number of unexplained ulcers of the penis, scrotum and vulva. Bacteriological and mycological examination microscopically and culturally have decreased the incidence of diagnostic errors. Nevertheless there still remain many lesions of unknown or doubtful origin. As a matter of fact, in the practitioner's office the clinical appearance of genital lesions will be the starting point in his diagnostic considerations.

The present chapter is to facilitate the practitioner's approach to genital ulcers. It seemed practicable therefore, to discuss the various forms of nonvenereal genital lesions which are known to be subject to ulceration.

The arrangement of this chapter does not encompass all possible ulcerative processes occurring in the anogenital region. For instance, ulcers due to deep fungus infection were discussed in Chapter 2 dealing with dermatomycoses of the genital area. Ulcers derived from vesicular or bullous skin diseases and herpetic eruptions required special discussions in Chapters 4 and 8.

B Ulcerations of Penis, Scrotum and Vulva Due to Mechanical, Thermal, Chemical or Physical Trauma

Traumatic lesions
Lesions suffered during sexual intercourse
Decubital ulcers
Self inflicted genital lesions
Lesions of the genitals by chemicals
Roentgen & radium burns

Traumatic Lesions

The management of *traumatic* lesions of the genitals (wounds, bruises, lacerations due to accidents, missiles or acts of violence self inflicted wounds including self mutilation of the insane or to birth trauma) belongs exclusively to the surgeon and gynecologist Bacterial ulcers secondary to gross trauma of the genital region, have been considered in other chapters.

Rather than such gross lesions however it is the more inconspicuous *apparently insignificant fissures and erosions of the penis and vulva which* may be of etiologic significance in genital ulcers

Lesions Suffered During Sexual Intercourse

Lesions suffered during *sexual intercourse* usually heal spontaneously and except for occasionally considerable bleeding, are practically of minor importance This refers especially to the common fissure of the *frenulum* in the male Under hygienic conditions this little lesion heals quickly but it may relapse following further sexual contact with the same female part ner Negligence, however clears the way for secondary infection which will require diagnostic consideration. In such cases small, atypical ulcers may form covered by a thin slough. Dark field examination for detection of spirochete pallida is indicated, and must be repeated if the first result is negative Difficulties in diagnosis may arise, particularly in cases in which patients have attempted a prophylactic" self treatment with concentrated antiseptics or silver nitrate.

Occasionally fissures of the introitus of the vagina may undergo trans formation into bacterial ulcers. Considerable bleeding in the presence of hymenal fissures should receive early medical attention to prevent com plicating infection.

Acute weeping ulcers or impetiginous lesions may develop as a result of *scratching* Simple excoriations may thus be transformed into irregular crusted lesions their configuration clearly indicating the effect of scratch-ing with the finger nails.

Decubital Ulcers

Decubital ulcers of the scrotum are not uncommon in association with decubitus of the sacral region developing during debilitating infectious

diseases, or after trauma of the spinal cord or other conditions, necessitating prolonged bedrest. A dry parchment like gray slough covers the ulcer accompanied by a more or less oozing secretion. Various superinfections may change the clinical aspect. The application of modern antibiotics is helpful in preventing complications. After recovery a sharp demarcation takes place followed by fresh granulations, epithelization and scar formation.

In rare instances, *scalding* of the female genitals results from mistakenly applied hot irrigation with resultant circumscribed erosions or ulceration. *Frostbite* of the male genitals has been observed during the winter campaigns in Russia in World War I in severely wounded, prostrated soldiers with torn clothing.

Self-Inflicted Genital Lesions

Serious damage may result from deliberate *constriction of the penis* by psychopaths. Ligatures with metal wires or with a ring pulled over the penis are followed by edema, which gradually increases to such an extent that removal of the foreign body becomes impossible, except by cutting or filing off the constricting band. Unless medical aid is obtained in time, the prolonged ischemia leads to gangrene. Dudek described constriction of the penis by a metal bolt. Extensive edema resulted and the removal of the bolt was possible, only following multiple scarifications and expressions of the edema fluid. A man of seventy-one years, of our knowledge had pulled a copper wire about his penis. When he was examined it was too late to prevent gangrene, even though the wire was filed off The whole shaft of the penis was involved. Following spontaneous slough of the necrotic tissues, the remaining defect resembled a surgical amputation wound.



FIGURE 71 Self inflicted amputation of penis due to copper wire constriction. The location of the catheter demonstrates the position of the urethral stump. (Callomon, F Die Nicht venerischen Genitalerkrankungen. G. Thieme, Leipzig, 1928, p. 78.)

Lesions of the Genitals by Chemicals

Lesions of the genitals by chemicals follow the inadvertent or mistaken use of caustic chemicals for prophylactic purposes. Intricate diagnostic and therapeutic problems may arise in cases of self inflicted chemical injury by *hysterical* persons or malingerers. Such injuries may result in round, oval or irregular ulcers, presenting a thin slough. Deeper necrotic lesions may develop into chronic ulcers. The clandestine application of cantharides and similar substances may produce blisters.

Continued appearance of vesicular eruptions in the genital region may suggest pemphigus or a fixed medicamentous exanthema. The association of such lesions with similar manifestations elsewhere on the body will not necessarily facilitate the detection of their true nature. The physician may be fooled for a long time.

Patients of this type may be extremely cunning, as evidenced by the case of a maiden of thirty-five years under our observation, who succeeded in producing by her own efforts a chronic, relapsing pemphigoid eruption that appeared at intervals on her arms and trunk. The true cause of this condition remained obscure, until it was discovered that a deep necrotic ulcer of the clitoris extending into the urethral meatus and causing a purulent cystitis had been induced by repeated self introduction of a catheter. For a period of months, this condition had been treated by a surgeon, a gynecologist and a general practitioner. During the cystoscopic examination necessitated by the bladder complication, a striking hypesthesia of the genital region was discovered. Clinical symptoms responded promptly to treatment and strict clinical supervision.

Becker and Obermayer reported almost complete destruction of the glans penis by long-continued application of a silver nitrate stick for a *supposed venereal infection.*

During World War I, malingerers or exhausted European soldiers, weary of war, often succeeded in simulating venereal infections by chemical production of ulcers of the penis or prepuce with mercury bichloride or other caustics.

The *differential diagnosis* of self inflicted genital lesions may be difficult *when no similar lesion can be found elsewhere on the body. Many of* these individuals cunningly retard the healing process by clandestine manipulations. However, the irregular distribution, the configuration and the characteristic necrotic crust of the lesions are suggestive of artificial ulceration. Occasionally there are tongue-shaped or striate areas of reddening (tell tale streaks) caused by the overflow of caustic chemicals. Gangrenous lesions due *to secondary infection must be distinguished from*

Vincent ulcers A careful general examination and the patient s history will often yield a clue for etiological diagnosis

Treatment: Artificially produced genital ulcers heal spontaneously with soothing applications applied during careful clinical observation usually requiring hospitalization Recurrences may occur after the patient s discharge from the hospital if adequate psychotherapy is neglected.

Roentgen and Radium Burns

Roentgen and radium burns of the anogenital region were not uncommon before modern advance in dosage and the proper selection of filters. However sequelae due to earlier treatment are still encountered Such



FIGURE 72. Radiation ulcer following -ray treatment of Grade I squamous cell epithelioma, associated with edema of right vulva—result of acut radiodermatitis of right inguinal region after -ray treatment of metastati inguinal lymph nodes.

lesions may be encountered in the perianal and perivulvar areas and may constitute sequelae of previous Roentgen treatment of pruritus ani et vulvae or of tumors. In their most dreaded form, the Roentgen ulcers, these residuals persist as a painful chronic condition presenting likewise the danger of possible malignant transformation Less conspicuous, and perhaps, likewise less resistant to therapy are the radium burns following a single over-dose or serial application of radium.

The *diagnosis* of Roentgen and radium ulcers is suggested by the patient s history or may be evident in the characteristic cutaneous changes of atrophy telangiectases, pigmentation, ulceration and warty growths.

Therapy of Roentgen ulcers has remained unsatisfactory up to the

present time Fundamental textbooks supply all possible information Many Roentgen ulcers are irreversible Others may improve under treatment. This does not exclude a spontaneous regression and epithelization of more superficial or small ulcers.

C. Ulcerations of Penis, Scrotum and Vulva Caused by Other Infections Than Venereal Disease

Tuberculous Ulcers
Chronic Tuberculosis of the External Genitals Lupus Vulgaris of the Vulva Penis and Scrotum; Scrofuloderma of the Inguino-genital Region
Lesions of the External Genitals in Leprosy

Diphtherial Ulcers
Ulcus Vulvae Acutum (Lipschütz)
Gangrenous Ulceration of the Genitals
Anthrax of the Genital Region
Genital Ulcers in Tropical Diseases

Tuberculous Ulcers

Acute forms: Primary tuberculosis of the penis, scrotum and vulva, contact infection circumcisional tuberculosis and secondary forms (tuberculosis cutis orificialis)

Two types of acute tuberculosis of the anogenital region must be distinguished (1) primary tuberculosis of the penis and vulva in individuals evidently free of tuberculosis up to the moment of local infection, and (2) tuberculosis secondary to other tuberculous lesions elsewhere in the body ("pseudo-primary tuberculosis complex)

Primary tuberculosis of the penis and vulva is a rare genital affection However unmistakable instances of primary genital tuberculosis have been reported, produced by direct bacillary transmission from a tuberculous individual to an obviously non tuberculous partner by sexual intercourse. E. L. Lewis for instance, in his special study of the literature (1946) collected twelve definite instances of acute tuberculosis of the penis due to sexual infection. M Schmid reported five cases of primary tuberculosis of the vulva developing after intercourse Three of the male partners were suffering from epididymitis tuberculosa, the remaining two partners had pulmonary tuberculosis.

The primary lesion, appearing about one week after infection, is a small nodular or pustular outbreak, subsequently progressing to a small irregular ulcer with serrated, slightly undermined edges. In this initial stage, microscopic changes show merely inflammatory tissue changes without any signs indicative of tuberculosis Slowly increasing in size a yellowish red ulcer develops slightly infiltrated and tender to touch. During the following week smears may show the tubercle bacilli. Epithelioid and

giant cells however appear later After a few weeks the inguinal lymph nodes may be involved. Until this time, when only the original ulcer is present, it is known as the tuberculous chancre."

Reports in the literature have long shown that primary tuberculosis of the cutis readily occurs after direct contact of a fresh wound with tuber culous sputum. A peculiar route of such infection has been described under the name "*circumcisional tuberculosis.*" Until the beginning of this century this mode of transmission was not extraordinary among the Jewish popula tion of Eastern European countries. In more recent times, only sporadic cases have been reported. E. L. Lewis, in his review of eighty nine cases of primary tuberculosis of the penis, recorded seventy two such instances, adding three personal observations.

Due to the Jewish rite of sucking the circumcized penis of the infant as a hemostatic measure, tubercle bacilli were transmitted with the saliva of a phthisical circumcisor The wound transformed into a large tuber culous ulcer Usually after two to four weeks, lymphadenitis and peri adenitis developed with caseation and perforation through the skin. Many infants died after generalization of the local infection.

A few definite instances of circumcisional tuberculosis have been observed in connection with *non*-ritual circumcision. Occasionally syphilis and diphtheria have also been transmitted to this region.

Acute tuberculosis of the *vulva* has been thoroughly described by Taussig and by Bender Beside the classical ulcerative form, there also occurs a hypertrophic variety which rare though it is, should not be over looked. French authors have described this type under the name "tuber culose hypertrophique non-ulcéreuse de la vulve. Chronic edema and elephantiasic tissue changes may persist for a long time with or without some later ulceration.

Recently Benjamin and Charnock (1949) reported primary hyper trophic tuberculosis in a twenty three-year-old woman with a blood stained discharge. A large, fungating, cauliflower-like mass covered the lower part of the labia, the fourchette and the posterior vaginal wall. Biopsy material showed a chronic inflammation with epithelioid cells, giant cells and numerous tubercles, which were also present in specimens taken from the affected inguinal nodes Koch bacilli were abundant. In this case there was dramatic response to treatment with streptomycin with complete healing after daily injections of 0.5 Gm. given for a period of six weeks.

Other clinical pictures have been reported as a primary tuberculous complex progressive with time. Resemblances to lupus vulgaris have been noted.

Secondary acute tuberculosis of the genitoanal region (tuberculosis

*cutis orificialis—tuberculosis of the mucous membranes) is a late complica*tion in advanced tuberculosis of the urinary tract or the intestines Multiple small irregularly shaped very painful ulcers develop around the urethral meatus, vulva or anus. Suppuration is slight and there is little tendency to bleeding Tubercle bacilli are demonstrable in smears. Spread of the in fection over larger areas may happen at any time When located in the anal region initial lesions may simply appear as longitudinal rhagades or fissures extending at times into the rectum These lesions are genuine inoculation ulcers (pseudo-primary tuberculous complex") Similar ulcers occur in and around the mouth and nose, in fulminating pulmonary tuberculosis.

Acute ulcers of the cervix, vagina or vulva are rare sequelae of tuber culosis of the internal genital organs, caused by a bacillary discharge coming down from the uterine cavity Hematogenous ulcers of the genital region are extremely rare (Lewis three instances among one hundred ten cases of acute tuberculosis of the penis)

Histopathology: Brunati distinguished three periods in the pathogenesis of primary penile tuberculosis (1) a small papule or pustule without induration (2) ulceration with slight induration, and (3) increase in size of the ulcer with inflammatory infiltration around the ulcer The second *stage produces ulcers very similar to chancroid* (chancre tuberculeux of the French authors) Microscopically the initial lesion shows a slight to moderate lymphocytic infiltration i.e merely non specific changes. Phagocytes containing bacilli do not appear before one to two weeks tubercle formation with giant cells developing later

Differential diagnosis: The first pustular outbreak may suggest herpes or pyoderma. The fully developed ulcer may be confused with venereal chancroid. The latter increases more rapidly in size with a tendency to coalescence in cases of multiple chancroid ulcers. Chancroid shows deeper undermined edges and the characteristic worm-eaten surface of the ulcer The distinction of the hypertrophic variety of acute tuberculosis of the vulva from papillomatous carcinoma or exuberant condylomata acuminata is impossible without microscopic examination of the tissue especially in *the absence of other symptoms indicating a tuberculous process elsewhere* in the body

The *prognosis* in primary tuberculosis of the penis and vulva is guarded because of the danger of generalization of the morbid process The patient's age is of great importance The prognosis is more serious in younger individuals and is most serious in circumcisional tuberculosis of infants when a massive bacillary infection gains entrance into an organism not sufficiently protected immunologically (Fejér)

In the secondary form i.e. that affecting the mucous membranes, the outlook is serious because of the extensive nature of the infection. The

fact that the infection has progressed to allow numbers of tubercle bacilli to invade the areas of the orifices of the body is indicative of the poor resistance of the host.

Treatment: A careful general examination is paramount in every case of acute tuberculosis of the genitals An early consultation with a phthisi ologist is strongly recommended regarding the possible presence of internal tuberculous disease

Local therapy such as surgical excision coagulation or radiotherapy is unsatisfactory and unpredictable in individual cases Local applications of vioform iodoform etc or analgesics are almost only of palliative value.

Considering the beneficial effect of large doses of *calciferol* (vitamin D) in cutaneous tuberculosis de Meuron used this treatment successfully in primary tuberculosis of the external genitals At the present time streptomycin given intramuscularly or/and locally seems to yield the best possible therapeutic results Fejér obtained complete healing of tuberculous genital ulcers in a ten year-old girl with pulmonary tuber culosis after vitamin D given for five months in combination with streptomycin (10 gm of streptomycin in all) The sputum became free of tubercle bacilli cultures on Coronini's medium, previously positive became nega tive A similar success resulted in Matthews's case of a seventy-seven year old woman with a non-healing perineal ulcer and renal tuberculosis (41 gm. of streptomycin given for six weeks, combined with a moderate dose of vitamin D_2)

It has been realized in the past few years that replacement of streptomycin with dihydrostreptomycin does not eliminate the auditory and vestibular toxicity of the former However combinations of equal parts of these two drugs may serve to diminish these reactions

Combinations of streptomycin with para aminosalicylic acid or isoniazid seems to offer greatest promise at this time

However when streptomycin or dihydrostreptomycin are used in the treatment of tuberculosis, consideration must be given to a possible development of resistance of the organism to the drug This is of special importance in late forms of the disease.

Chronic tuberculosis of the external genitals; Lupus vulgaris of the vulva, penis and scrotum; Scrofuloderma of the inguino-genital region: *Lupus vulgaris* of the vulva, penis and scrotum is the rarest form of tuber culosis of the external genitals. Exceptionally this part of the body may be one of the locations of widespread lupus vulgaris. Less uncommon is involvement of this area in lupus expanding from neighboring districts down to the genitoanal integument

According to the peculiarities of the cutaneous structure of the ex ternal genitals various clinical forms of lupus vulgaris may develop the

hypertrophic form with chronic edema, elephantiasic thickening and proliferations in the anoscrotal region or the serpiginous scaling type in the pubic region and on the buttocks

Lupus vulgaris of the *vulva* may produce solitary irregular ulcers near the clitoris or the posterior commissure, presenting diagnostic difficulties such reports are scarce in the literature (Bender Fessler) Very rare is the ulcerating type of lupus vulgaris (lupus exulcerans) of the *scrotum* and *penis* The mutilating form of lupus was described by Kinzel in the case of a six year-old boy with widespread lupus vulgaris (nose, face, thighs) the major part of the glans and shaft of the penis were destroyed except for a small stump



FIGURE 73 Lupus vulgaris, gluteal region. (Dermat. Clinic, Univ Leipzig, Prof Dr J H Rille)

Proceeding from tuberculous inguinal glands or pelvic bones, *colliquative cutaneous tuberculosis* (scrofuloderma) may develop associated with caseation and abscess formation (gommes scrofuleux of the French authors) indolent sinuous ulcers with undermined borders may result in radiating scars

DIFFERENTIAL DIAGNOSIS Lupus squamous and serpiginosus of the genital and pubic region must be differentiated from psoriasis, which will be excluded by the absence of the apple jelly colored tuberculous nodules, readily demonstrable by glass pressure in the marginal zones of lupus vulgaris

The serpiginous type of lupus demands also distinction from tertiary forms of cutaneous syphiloma, both conditions showing a tendency to central healing with peripheral progression But the induration of syphiloma,

the lack of tuberculous nodules, the history and serologic tests for syphilis give essential clues for diagnosis. However positive seroreactions do not exclude a possible coincidence of syphilis and tuberculosis.

Solitary ulcers of lupus vulgaris of the vulva may be confused with malignant ulcers (ulcus rodens) but the borders of epitheliomatous ulcers are more indurated and usually rolled. Usually lupus exulcerans shows a more abundant secretion than do neoplastic ulcers. In particular the papillary form of lupus vulgaris, occurring in the perianal region or on the scrotum, requires differentiation from malignant growth.



FIGURE 74 Tuberculosis colliquativa (scrofulous gumma) of the genitalia with involvement of inguinal lymph nodes. (Dermat. Clinic, Leipzig, Prof. Dr J. H. Rille)

The importance of biopsy and histological examination in diagnostically uncertain cases of chronic tuberculosis of the genitals is evident. The exceptional incidence of *papulonecrotic tuberculides* on the glans penis, first described by Hellerstrom (1943) and by Bafverstedt and Hageman (1948) has been recently confirmed by Granroth (1952) He described two new instances showing all characteristics of this late manifestation of tuberculosis in hyperergic individuals after an earlier infection.

Usually papulonecrotic tuberculides affect the extensor surfaces of the extremities, the fingers or the face. History clinical aspect and a positive tuberculin reaction will point to the origin of the characteristic scars left on the penis which will hardly be confused with the more irregularly shaped scars resulting from soft chancre (see Fig. 75)

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FIGURE 75 Papulonecrotic tuberculide, lesions of glans penis. Note depressed scars. (Granroth, T *Acta dermat venereol* 32 116 supplement honoring Haxthausen.)

THERAPY In the treatment of *chronic* cutaneous tuberculosis, the combined administration of streptomycin and para aminosalicylic acid has been tried with remarkable results.

Calciferol has been of great value, beginning with doses of *150 000* units daily for about three or four months and then decreasing to 100 000 units daily Because of slow response to treatment, calciferol must be administered for many months. During this time, careful watch for toxic reactions is essential (nausea abdominal pain, diarrhea)

Isoniazid (Nydrazid, Squibb) given orally over long periods, with daily doses of 2 to 10 mg per kilo of body weight, caused minor side-effects in a small proportion of the cases (Rubin and Burke, 1953) Nydrazid in combination with streptomycin seems to be more appropriate than either compound alone Equal results have been reported by German clinicians using the analogous compound Neoteben (Domagk) Both the American and the German compounds offer great promise in the treatment of lupus, tuberculosis verrucosa and colliquativa. As Kimmig showed, the maximum of blood concentration is reached four hours after intake of *100 mg of neoteben followed by rapid* excretion in the urine during forty-eight hours. A daily dose of 0 4 Gm. given in four single doses of 100 mg proved well compatible over many months. Side effects (anorexia,

nausea, thirst) may occur but need not necessarily recur after re-administration. However reservation appears necessary concerning the dosage of these isonicotinic acid hydrazids, since Ehring Heimeyer and other investigators observed mental disturbances following prolonged administration (0.8 mg per kilo of body weight had been given by Ehring in the respective cases) Further studies may determine the minimal dosage sufficient for a most favorable effect.

Lesions of the External Genitals in Leprosy

Incidence: *According to prominent leprologists such as* A. Hansen and A. Neisser cutaneous lesions of the genitals in leprosy are extremely rare. This opinion prevailed, until Glueck described nodular lesions of the penis in ten of forty male lepers. More recently Fox and Knott (1934) found leprous nodules on the scrotum and penis in four of thirty four patients.

In comparison with other genito-urinary manifestations of leprosy such as orchitis, epididymitis and testicular atrophy the lesions of the penis, scrotum and vulva are indeed rare They are found chiefly in patients with the nodular type of leprosy less frequently in those with mixed types and occasionally in patients with the macular type of the disease (Grabstald and Swan, 1952) Serra, in an elaborate study based upon one hundred and *seventy two cases of leprosy recorded vulvar lesions in 13 per cent, pre*putial lesions in 10 per cent, lesions of the coronary sulcus in 5 per cent and of the glans in 3 per cent of all cases

Clinical appearance: According to Glueck, the nodular genital lesions in lepers appear either as distinct nodules of the size of a kernel of corn to that of a hazelnut or as yellowish brown to brownish-red infiltrations of various *shape and consistency When fully developed, they may simulate* primary chancre and may require differentiation from syphilis.

Differential diagnosis: In the absence of other symptoms indicating either syphilis or leprosy the differentiation of the two conditions may prove difficult. The demonstration of Hansen's bacillus is of foremost importance In evaluating the significance of serological tests for syphilis, reservation is necessary owing to the frequent incidence of false positive reactions. Grabstald and Swan cited statements of the United States Public Health Service according to which 45 to 59 per cent of presumably nonsyphilitic patients with leprosy showed false positive serum reactions for syphilis. According to these same authors, approximately half of the patients admitted to the National Leprosarium at Carville Louisiana, had been diagnosed as having syphilis some time prior to admission (literature cited by Grabstald and Swan) Similarly Balbir Singh recorded a high incidence of false positive Wassermann and Kahn reactions in a series of

sixty four lepers Such reactions were more frequent in patients with nodular leprosy than in those with macular leprosy

One of Serra s cases is worthy of general attention because in addition to a clear venereal history the patient presented clinically a hard nodular lesion on the coronary sulcus associated with inguinocrural adenopathy There were no other lesions elsewhere on the body Serologic tests for syphilis were negative On microscopical examination, the secretion from the lymph glands was found free from pallidae, but contained masses of Hansen s bacilli which were also demonstrated in biopsy specimens (carbolfuchsin methylene blue staining) About a year before admission, this patient had sexual intercourse with a woman known to have leprosy

Serra presents this case as one of the rare incontestable instances of a primary genital leprous infection due to sexual contact. Such observations *are most rare Lampe and Boenjamin have issued a general warning against* drawing definite etiological conclusions from the data available in an uncertain individual case of this kind considering the length of time elapsing since the contact of the non leprous with the leprous individual (two to twenty years)

The value of the immunological *lepromin test* (Mitsura, 1916) in the differentiation of leprous lesions from similar cutaneous affections has been emphasized by many leprologists Intradermal injection of a test material obtained from ground leprosy nodes produces (1) an early reaction of mild character after one or two days to disappear after three to four days, and (2) a late reaction causing larger nodules and, subsequently ulcerations. The late reaction represents the typical Mitsura reaction which reaches its climax seven or more days after inoculation to disappear slowly during three or four weeks (Dharmendra)

The *treatment* of leprosy has improved with the use of the sulfones in recent years It will be some time however before complete evaluation can be made Isoniazid also offers some promise in the treatment of this disease.

The *histopathology* of cutaneous leprosy and the *therapy* of this disease are thoroughly discussed in the pertinent literature.

Diphtherial Ulcers

Genital ulcers, caused by the corynebacterium diphtheriae, occur predominantly in children, but are not rare in adults especially in women. They may appear on the penis, scrotum or vulva, including the vulvar mucosa. *Primary* diphtheria of the genitals is rare Usually diphtherial ulcers are secondary to diphtheria of the throat or nose, due to direct transmission of the infectious material to the genitals. Abrasions or open

wounds furnish the portals of entry Bacterial ulcers of other origin may be subject to superimposed diphtherial infection

Genital diphtheria produces either solitary or more frequently multiple lesions, which may be distributed over the genitoanal region and the inguinocrural folds of the lower abdomen. In some cases of primary genital diphtheria, the source of infection may remain obscure In several instances contagion could be traced back to carriers in the family of the patient. Or the patient himself may have been a carrier before appearance of the genital lesion. Primary genital diphtheria may be followed by diph



FIGURE 76. Cutaneous diphtheria of the genitalia and the lower bdomen. Abundant diphtheria bacilli in smears. (Dermat. Clinic, Breslau, Prof Dr J Jadassohn.)



FIGURE 77 Cutaneous diphtheria of penis. (Moulage, Clinic Breslau, Prof Dr J Jadassohn.)

theria of the throat in the same patient or persons coming into contact with him

Klebs-Loeffler bacilli are readily demonstrable in smears or cultures taken from the genital lesions in smears, they may be associated with streptococci, staphylococci, and pseudodiphtheria bacilli.

Diphtherial ulcers of the genitals vary in shape and size. Besides the typical ulcer with its pseudomembranous grayish white coating, pustular and impetiginous lesions may form Or deep necrotic ulcers may be seen covered by an adherent yellowish to brown or gray leathery slough. The margins are infiltrated but not markedly undermined, and the lesions are surrounded by a dark red area. Fresh diphtherial ulcers are painful. The inguinal glands are swollen firm and tender Edema of the prepuce

scrotum and the labia majora may be intense. Rauscher described "balanitis diphtherica" in an infant with diphtheria of the throat; there was an intensive swelling of the penis and *bullous* edema of the scrotum.

The healing process sets in with formation of fresh red granulations after shedding of the necrotic scab. However, healing may be retarded for several weeks, even after antitoxin therapy. Baccaredda found Klebs-Loeffler bacilli still present on the vaginal mucosa of a child four months after recovery.

It is known that the diphtheria bacillus can thrive as an epiphyte on the healthy skin. It becomes pathogenic when irritation, trauma or eczematoid dermatosis favors a virulent bacterial growth. An *eczematoid form* of genital diphtheria may occur as a complication of intertriginous eczema in





FIGURE 78 FIGURE 79

FIGURE 78. Pseudodiphtheric lesions of the glans penis. (Courtesy of Prof. Dr. G. B. Cottini, Catania.)
FIGURE 79. The same patient as Fig. 78.

children and has likewise been observed in association with perioral, *perinasal or periauricular eczematous eruptions.*

All serious symptoms and complications occurring in diphtheria of the throat may also develop in primary diphtheria of the genital region. In the majority of cases, high fever accompanies the onset of the infection. Also late complications such as post-diphtherial pareses, heart failure, disturbances of accommodation, have been reported as sequelae of primary genital diphtheria.

In contrast to true diphtherial ulcers, pseudodiphtherial ulcers of the genitals remain usually localized to the site of entry and never cause constitutional symptoms. They are never followed by paresis or heart trouble. Pseudodiphtheria bacilli occur as saprophytes on the vulvar and vaginal mucosa.

Primary diphtheria of the *penis* has been described in both adults and children. Most frequently the infection was limited to the preputial sac,

producing deep, extensive, infiltrated grayish-yellow lesions on the edematous prepuce and glans. Impetiginous crusts may cover the preputial lesions, and when detached disclose irregular ulcers with a yellowish white coating. Princing observed multiple diphtherial ulcers on the phimotic prepuce of a man of twenty-eight years. In this case the sister and wife of the patient were carriers. Klebs-Loeffler bacilli were demonstrated in smears from the healthy vagina of the wife.

Primary diphtheria of the vulva, when involving the labium majus, results in a rigid swelling and widespread infiltrated reddening. Typical ulcers with pseudomembranous coverings or gangrenous patches are found in vulvar diphtheria, sometimes associated with pustular or eczematoid lesions.

A most serious form of diphtheria of the vulva, now extremely rare, is the *puerperal diphtheria* observed in women suffering from diphtheria of the throat at the time of delivery. The classic description by Bumm (1895) refers to a puerpera of twenty-one years of age, delivered by forceps by a doctor who had previously treated several children with diphtheria. Three days postpartum, a high fever indicated a serious infection. The aspect of the vulva did not suggest a streptococcal infection. The labia majora and minora were covered with irregular shiny white, thick uneven membranes, surrounded by a red area and extending up into the vagina to the cervix. Instead of streptococci diphtheria bacilli were found in the smears and were identified by culture. Antitoxin treatment proved successful. H. W. Freund reported puerperal diphtheria, localized on a freshly sutured perineal rupture in a recently delivered woman, who was suffering from diphtheria of the throat.

Differential diagnosis: The differentiation of genital diphtherial ulcers from venereal chancroid, ulcus gangraenosum penis or vulvae, and balanitis gangraenosa depends essentially on the demonstration of diphtheria bacilli in smears as well as in culture. The bacteriological differentiation between diphtherial and pseudodiphtherial infection may be difficult. Animal inoculation will be decisive.

Therapy: The results of serum therapy are generally good, although not uniform in genital diphtheria. Judging from the literature the majority of cases respond to doses of antitoxin similar to those used in diphtheria of the throat. Its combination with penicillin seems most effective. Early treatment is imperative. A slowly progressing recovery from genital diphtheria may demand a higher dosage of antitoxin.

Ulcus Vulvae Acutum (Lipschutz)

In 1912, B. Lipschutz gave the first clinical description of a well characterized form of acute ulcers of the vulva, with constant findings of a

gram positive bacillus, which he named Bacillus crassus. The fact that this lesion occurred predominantly in intact virgins, and not infrequently in children, excluded a venereal infection from the beginning. The original name ulcus vulvae acutum has held its ground in the international nomenclature as an etiologically non-committal term. In 1913 G Scherber published analogous observations and additional bacteriological studies. He furnished incontestable proof that Lipschütz's B crassus is identical with the Doederlein bacillus ("Scheidenbacillus) most common saprophyte of the normal vagina.



Figure 80 Ulcus acutum vulvae (Lipschutz) (Courtesy of Prof Dr M Monacelli.)



Figure 81 Ulcus acutum vulvae (Lipschutz) (*Dermatologische Studien*, ed. by Unna-Rille. Leipzig, 1923 Fig —)

Both investigators published their experiences and new contributions from the literature in Jadassohn's Handbuch, Vol. XXI (Lipschütz, 1927) and in Arzt Zieler's Handbuch (Scherber 1935)

The ulcers may be single or multiple, the initial lesion being usually located on the inner aspect of the labia minora. Varying in number shape, distribution and painfulness, the lesions present all the features of an infectious process A febrile onset has been reported in some cases, but the majority run an afebrile course

The age of these patients varied from ten to twenty years occasionally infants and young married women were afflicted and exceptionally unmarried women of more than thirty years.

Lipschütz, in his original description distinguished three clinical types, as follows

(1) A *gangrenous* form (the "diphtheroid necrotic form of Scherber) characterized by a stormy onset with chills, fever and burning pains. One or more round to oval erosions of pea to penny-size, appear on the inner aspect of the labia minora and other parts of the vulvar mucosa within the first two to four days. The lesions are covered by an adherent grayish-yellow to bluish black scab, which after another three days, is replaced by a yellowish or gray fibrinous coating. A purulent secretion covers the red and swollen vulva. Recovery takes place with formation of fresh red granulations and rapid epithelization after a total course of about two weeks leaving inconspicuous scars.

(2) A milder usually afebrile form, simulating venereal chancroid (*venereal*" form) These ulcers are soft, more shallow and of a round or polycyclic shape with sloping or undermined margins, but without the worm-eaten aspect of chancroid ulcers A dark red swelling of the involved labia accompanies the painful condition Multiple ulcers may affect the anterior and posterior commissures the prepuce of the clitoris and occasionally the adjacent perineal and perianal skin. Relapses may occur once or at intervals The course of this form is more subacute and usually extends up to one month due to a more successive appearance of lesions. It seemed noteworthy that in relapsing cases B crassus continued to be demonstrable during the intervals.

(3) A "*miliary* type, presenting numerous tiny not more than pinhead sized ulcers, which develop almost over night. The lesions are painful and may involve the external aspect of the labium majus. Occasionally the surrounding areas of the skin are involved (inguinocrural folds, perineum) In the majority of cases, these eruptions appear in association with ulcers of the venereal" type.

Judging from the literature, autoinoculation as well as experimental transmission of pus from ulcers to other individuals, have always yielded negative results. In cases observed in young married women, transmission to the husband has not been reported. Scherber mentioned the incidence of ulcus vulvae acutum with findings of B crassus in two infants in the same family Thus the infectious nature of Lipschütz ulcers appeared evident their contagiousness, however if existing at all, seemed to be insignificant.

B crassus, so-called Doederlein s bacillus is a straight, short thick, non motile rod with truncated ends, staining with aniline dyes. It is a gram positive organism. Longer forms occur sometimes arranged in chains. On culture B crassus thrives in both aerobic and anaerobic media. It belongs to the lactic acid forming bacteria. It is abundantly found in smears, sometimes intermingled with banal bacteria, but always the prevalent type.

Histologically vascular changes dominate the picture. The walls of the vessels show edema and swelling of the endothelial lining. A dense inflammatory infiltration extends deeply down to the corium. The upper parts of the section show numerous, partly intracellular bacilli and the uppermost stratum shows necrosis. The deeper layers of the cutis, although markedly involved in the infiltration, contain no organisms or occasionally a few bacilli.

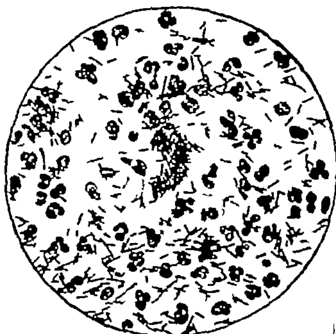


FIGURE 82. Bacillus crassus, Lipschutz, smear preparation, magnified × 1800. (*Dermatologische Studien*, Fig. 12.)

Etiology: Ulcus vulvae acutum presents all the characteristics of an infectious process. The constant finding of B. crassus offers a useful diagnostic hint. Nevertheless, the question arises whether this organism does indeed act as a specific pathogenic agent. Checking the international literature, we still encounter differences of opinion. Only hypotheses have been offered in answer to the question as to which circumstances may transform the saprophytic B. crassus (so-called Doederlein's bacillus) into a virulent organism.

Important arguments appear to refute its specificity. Already in the earlier literature and increasingly in our times, instances have been reported of ulcus acutum in combination with aphthosis of the mouth and with cutaneous symptoms such as papulovesicular eruptions and/or with erythema multiforme exudativum occasionally complicated by an abacterial

form of pneumonia (Hammerschmidt and Korting, 1949) This coincidence has given rise to the interpretation of ulcus vulvae acutum as a condition possibly related to stomatitis aphthosa, ectodermosis pluriorificialis and certain forms of erythema multiforme. We refer to Chapter 5

This hypothesis has been widely advocated. Even the earlier authors reported Lipschütz ulcers and aphthosis of the mouth in the same individual (Lipschütz himself Carol and Ruys Kumer recently Andrews, 1946) However B crassus, always present in the genital ulcers, was never demonstrable in the oral lesions. As in ulcus vulvae acutum, attempted transmission from oral aphthae to the skin always yielded negative results. B crassus is occasionally found also in other lesions as for instance in typhoid ulcers. It has been suggested that possibly B crassus may act here as an accessory factor in decreasing the tissue resistence against some unknown infection (virus infection?) An onset with chills and fever was common in all the above mentioned cases with concurrent oral lesions. There remains an open field for further investigation.

Differential diagnosis: The differentiation of Lipschütz ulcers from venereal chancroid has been previously discussed the presence of B crassus in the former and of the Ducrey bacillus in the latter will clinch the diagnosis Vincent ulcers and vulvitis erosiva circinata et gangraenosa are characterized by fusospirochetosis

Genital ulcers caused by diphtheria bacilli differ from ulcus vulvae acutum by their adherent grayish white coating they are deeper infiltrated and surrounded by a more intense reddening The inguinal glands in genital diphtheria are indurated and always painful. The identification of Klebs-Loeffler bacilli and the general condition of the patient confirm the diagnosis. Also pseudodiphtherial ulcers must be excluded. As Lipschütz stressed the presence of B crassus is essential for the diagnosis of ulcus vulvae acutum.

Fresh Lipschütz ulcers may be mistaken for herpetic lesions unless the herpes eruption involves the labia majora and the surrounding skin simultaneously Residues of vesicles, the shape and grouping of herpetic erosions and their transitory nature will reveal their origin.

Before the monographs of Lipschütz and of Scherber E. Finger in his lectures classified ulcus vulvae acutum i.e., the venereal" type as described by Lipschütz, as pseudotuberculous" genital ulcers, so as to exclude tuberculosis from the beginning.

Treatment: Ulcus vulvae acutum is a self healing disease provided hygienic conditions are maintained. The uneventful course can be supported by rinsing with Sol. boric acid 3 per cent, or Sol. potassium permanganate (1 3000 to 1 5000) or in necrotic ulcers, by swabbing with hydrogen peroxide Febrile cases require bed rest.

Gangrenous Ulceration of the Genitals

Gangrenous ulcers may develop from traumatic lesions after accidents, injury by gunshot or explosive missiles *Gangrenous transformation of any* ulcer may be induced by secondary infection with streptococci, staphylococci, diphtheroids vibrioid (fusiform) organisms spirochetes or other infectious germs Secondary or mixed infection may transform a chancroid or syphilitic chancre into a gangrenous ulcer Infectious organisms transmitted from gangrenous lesions elsewhere on the body can produce gangrenous ulcers of the penis or vulva. On the other hand, it is possible for primary gangrenous ulcers of the genitals to provide a starting point for gangrenous processes elsewhere on the body surface.

Fusospirochetosis as a cause for genital gangrene: The oral cavity is the main reservoir of fusiform bacilli and certain spirochetes. These organisms also thrive as parasitic elements in the preputial sac, especially under the anaerobic conditions of phimosis. They may become virulent and pathogenic when the body resistance has been lowered by disease or malnutrition

The *symbiotic* activity of these two organisms is responsible for various *gangrenous processes, such as Vincent's disease of the mouth, the ulcus* gangraenosum (phagedaenicum) penis or vulvae" the gangraena nosocomiale" of the genitals and "balanitis gangraenosa. Constant findings of fusiform bacilli and certain spirochetes (sp refringens and sp balanitis) are characteristic of all these affections The ratio of incidence of these germs varies in individual cases spirochetes may outnumber fusiform bacilli and vice versa. As a rule, this symbiotic pair prevails among concomitant bacteria such as smegma bacilli, various types of cocci, or filiform bacilli. Fusospirochetosis is the most common cause of genital gangrene.

The pathogenicity of fusospirochetosis has been demonstrated experimentally Vincent's ulcers of the penis have been produced by inoculation of the glans and prepuce with material from stomatitis ulcerosa *(Queyrat)* Cirillo substantiated the buccal origin of gangrenous genital ulcers in twenty cases McCormac observed vulvitis gangraenosa following intercourse with a partner suffering from stomatitis membranacea, who used his saliva as an ante-coitum lubricant In a similar case reported by Milian gangrenous ulcers of the vulva were produced by contact infection from the husband with a kiss.

Scherber's observation of the infection of two men from the same woman has definite significance In both cases, gangrenous lesions of the penis followed a similar incubation period (four days after intercourse)

Ulcus gangraenosum (phagedaenicum) penis et vulvae: Matzenauer (1901) was the first to stress the identity of the phagedenic ulcer of Neu

mann and the "ulcus gangraenosum" penis. Subsequently Rona's gangraena nosocomiale of the genital region was proved to be another variant of this group of ulcers.

After an initial stage of fibrinous exudation, one or more round ulcers form. The uneven base of the ulcer is soon covered by a diphtheroid, grayish-brown to greenish pseudomembrane. If the exudate is serous the



FIGURE 83. Ulcus gangraenosum, fusospirotrichosis. (Courtesy of Prof Dr G B Cottini, Catania.)



FIGURE 84 Ulcus phagedaenicum of the clitoris (fusospirochetosis) (Dermat. Clinic Frankfurt, Prof Dr O Gans.)

resulting crust is more gelatinous. The mechanical or spontaneous detachment of the crust causes slight to intense arterial bleeding. The ulcer may increase to a large gangrenous lesion, having a foul odor The condition is painful, especially when developing in a phimotic preputial sac. A dark inflammatory redness develops with intense swelling. Surgical opening of the preputial sac becomes imperative and in many cases from the older literature sufficed to bring relief and improvement simply by exposing the anaerobic micro-organisms to the air

Today the powerful effect of *antibiotic treatment* shortens the course dramatically preventing deeper destruction and lessening the need for extensive surgical procedures

Balanitis gangraenosa (Corbus and Harris Scherber and Müller) chiefly affects the prepuce and glans. Multiple small ulcers may be observed spreading along the coronal sulcus and producing an abundant



FIGURE 85. Ulcus phagedaenicum of glans penis. (Dermat. Clinic, Naples, Prof Dr M. Monacelli.)

purulent secretion. The prepuce is edematous. The inflammatory reaction may involve the entire penis and the adjacent pubic region. Unless treated, the gangrenous ulceration may invade the spongiose tissue of the glans, and exceptionally the adjacent corpus cavernosum. In one of our own patients who was suffering from balanitis gangraenosa, deep undermining of the tissue resulted. This very rare complication was known in the earlier literature as cavernositis dissecans.

Balanitis gangraenosa usually afflicts patients between nineteen and twenty-five years of age.



FIGURE 86. Balanitis gangraenosa. (G Scherber Handb. Haut-u. Geschlechtskr vol. XXI, p 285 Fig. 5 Springer Berlin, 1927)

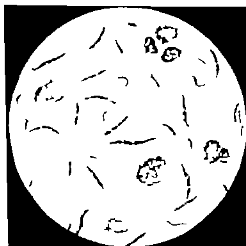


FIGURE 86a. Fusospirochetosis in Plaut Vincent's angina. Borax-methylene blue staining (Black-white reproduction. Callomon, Die Nichtvenerischen. *Genitaler krankungen*, G Thieme Leipzig, 1928, Fig. 45.)



FIGURE 87 Perforation of the prepuce f llowing lcus gangraenosum, associated with balanitis erosiva. (Dermat. Clinic, Frankfurt, Prof Dr O Gans.)

The histological findings in ulcus gangraenosum (phagedaenicum) penis and in balanitis gangraenosa are identical. Intense inflammation is often associated with hemorrhage, with loss of cell contours and nuclei in the necrotic area, up to complete coagulation necrosis. As a rule fusospirochetosis can be demonstrated in smears by dark field examination and in stained preparations.

Balanitis erosiva circinata, first described by Bataille and Berdal (1889) has been generally recognized as a superficial form of balanitis gangraenosa, showing identical bacteriological findings. Bataille and Berdal succeeded in producing typical necrotizing lesions experimentally by inoculation with pus from the coronal sulcus. These lesions proved transmissible to other cutaneous areas by experimental inoculation of patients. Scherber demonstrated the transmissibility in humans.

Balanitis erosiva circinata may develop spontaneously but usually develops following intercourse. After an incubation period of thirty six to forty-eight hours one or more small, round, bright red, pinpoint to lentil sized erosions form predominantly on the inner preputial leaf and the coronal sulcus, sometimes including the glans. They are surrounded by a characteristic, small whitish margin, a residue of the necrotic epithelium. A yellowish slough covers most of the lesions. The latter may coalesce to form larger erosions, especially along the coronal sulcus, which then presents an annular eroded lesion covered with pus After wiping off the foul-smelling secretion, the circinate outline with its whitish margin is readily demonstrable. Deep ulcers are uncommon.

The climax is reached between the fourth and eighth day after onset. Spontaneous healing supported by simple rinsing and washing not infrequently takes place within four to five days.

Histologically a homogenous or firmly granulated mass replaces the superficial epithelial layers edema and inflammation are limited to the underlying papillary body

Vulvitis erosiva circinata corresponds precisely to a similar condition in the male, although much less common. This is easily understood when considering the absence of ventilation in a phimotic preputial sac, which thus constitutes an ideal location for proliferation of anaerobic bacteria. Occasionally some deeper lesions are found intermingled with the typical circinate erosions.

Differential diagnosis Usually the differentiation of these lesions from other necrotizing affections of the penis and vulva will depend upon the constant finding of fusiform bacilli in association with spirochetes in the smears Their prevalence among concomitant micro-organisms is important.

B fusiformis is a small, curved or sickle-shaped, very motile rod, often showing central vacuoles in stained preparations It differs from the diphtheria bacilli by the absence of the club-shaped endings of the latter It is easily stained with aniline dyes (methylene blue) but is unstable to gram-staining Gram-positive staining seems to prevail in the initial stages possibly corresponding to the actual state of virulence The symbiotic spirochetes are easily distinguished from T pallida by their more dis-

tinct appearance, a different number of windings, and a more or less different motility

It must be kept in mind that even a constant absence of T pallida in the smears taken from a gangrenous ulcer does not exclude the possibility of a mixed infection, especially in the presence of abundant bacteria in the preputial flora, which may overshadow the simultaneous presence of T pallida.

Occasionally a necrotizing, syphilitic sclerosis may simulate a phagedenic ulcer of the penis or vulva, until the increasing induration, the painless course, and the involvement of the regional glands point to a syphilitic infection. In the search for a possible mixed infection, puncture of the inguinal glands may prove helpful in demonstrating the presence of T pallida, at a time when serologic tests for syphilis are still negative A positive serologic test for syphilis, in the absence of T pallida does not, on the other hand, exclude the possibility of a gangrenous ulcer in a patient with previously existing syphilis Occasionally a phagedenic ulcer of the penis must be distinguished from a malignant ulcer The acute inflammatory onset of an ulcus gangraenosum penis differs markedly from the insidious development and slow progression of a malignant neoplasm. Biopsy offers a definite clue for diagnosis

Erosions caused by balanitis or vulvitis erosiva circinata may be mistaken for herpetic lesions. In the case of herpes genitalis, residues of vesicles and the transitory character of a herpetic eruption would indicate its nature.

Differentiation from chancroid presents little difficulty because of the pain rapid increase in size and undermined borders of the soft chancre, and the worm-eaten appearance of the base of the chancroid ulcer Pains are more likely to diminish in severity in the course of a phagedenic ulcer whereas in an untreated ulcus molle, pains become increasingly severe. The demonstration of Ducrey bacilli provides further evidence of chancroid infection.

THERAPY In the presence of phimosis, surgical treatment is imperative. Free access of air facilitates the control of anaerobic infections as well as the local application of antiseptics. Before the era of antibiotics, the local application of hydrogen peroxide dilutions also served to expose anaerobic organisms to oxygen. Today the powerful effects of penicillin or Tetracycline shorten and insure the healing process. Penicillin will promptly arrest and cure balanitis gangraenosa, ulcus gangraenosum penis and vulvae as well as Vincent's disease of the mouth. Tetracycline equally efficient has the added advantage of permitting oral administration and a low toxicity Blake *et al* noted dramatic cure in a combined case of buccal and penile Vincent ulcers (initial dose 1 0 gm t.i.d., followed by

0.5 gm t.i.d. for four days and 0.25 gm. four times daily for one day) Organisms had completely disappeared after twenty four hours, and healing of all lesions was accomplished by the sixth day of treatment.

Balanitis pustulo-ulcerosa, du Castel, described in 1889 appears clinically closely related to balanitis circinata and gangraenosa. The onset is marked by the appearance of pointed nodules or small pustules on the glans and inner leaf of the prepuce Some of these lesions may disappear spontaneously but most of them develop into painful, irregular gray to yellowish ulcers covered by an adherent diphtheroid slough. They may coalesce to form polycyclic lesions producing a slight serous or purulent secretion

In the smears and subsequently by culture Pautrier and Rietmann found gram negative coccobacilli suggested specificity However autoinoculation and transmission to rabbits yielded negative results. These authors and in two additional cases also Lévy Bing and Garnay stressed that neither spirochetes nor Ducrey bacilli were found in the smears. The question remains whether or not du Castel s form of balanitis represents a special variant of acute bacterial balanitis.

According to Pautrier and Rietmann this condition likewise differs markedly from herpetic erosions and from chancroid.

Diffuse forms of genital gangrene: Extensive diffuse gangrene may involve the genital region secondary to septic *thrombophlebitis* of the pelvic veins Gangrene may spread over large areas, including the lower abdomen Such cases are rare but always fatal.

Of special practical importance is the genital location of *diabetic gangrene* that occurs in advanced untreated diabetes. This condition may develop with or without a preceding inflammatory affection of the glans or prepuce especially in cases of phimosis, and predominantly in patients of advanced age The condition may spread rapidly with formation of large malodorous sloughs The secretion may be slight or abundant.

This painful complication is rarely encountered, now that insulin treat ment and systematic control of diabetes have largely contributed to prevent and manage diabetic complications. A pre-existing balanoposthitis may favor the proliferation of gangrene-producing bacteria in the preputial flora, but gangrene may also develop spontaneously in diabetics as a result of vascular changes in other locations.

Erysipelas gangraenosum occurs not infrequently when the scrotal skin is involved in erysipelas or is the starting point. Gangrene follows rapidly the initial reddening and swelling of the scrotum At first glance the lesions may appear like those of Fournier s gangrène foudroyante. Both diseases are accompanied by fever chills and prostration. However in erysipelas peripheral progression soon shows the characteristic expansion

of reddened circumscribed extensions. This form of erysipelas has become very rare since the advent of antibiotic therapy.

Spontaneous gangrene of the scrotum ("gangrène foudroyante" Fournier 1884). This serious condition was thoroughly studied by Milian (1917) and his pupil Nativelle (1930). Comprehensive reviews and case reports were presented by Balog and Cerqua, Gibson, Robinson (1946) and Randall (1950).

Three cardinal symptoms form the clinical picture: (1) a sudden onset, surprising men in their best state of health, (2) rapid progression of gangrene over large areas of the scrotum, and (3) the absence of other factors leading to gangrene. After a stormy onset with fever, chills, prostration and violent pains, there develops an immense swelling and reddening of the scrotal integument with gangrene developing within the first twenty-four hours. It may progress to the penoscrotal fold and to the penis but *never involves the whole shaft. Destruction of the scrotal skin may be so* complete as to lay bare the testicles, which are themselves, however, never involved.

During the pre-antibiotic era, septicemia and a fatal issue were not uncommon results, but even then spontaneous healing was occasionally observed. For this reason, even before antibiotics Buschke issued a warning against precipitate radical surgery.

Balog and Cerqua described this form of gangrene in an Egyptian of forty-five years. Figure 88 shows all the characteristics of the fully developed disease: the scrotum swollen to the size of a child's head, a grayish to blackish-brown slough covering the affected portion of the scrotum, large areas of the penile skin involved except on the glans. A foul odor was noted. Spontaneous detachment of shreds of necrotic tissue revealed the extent of destruction: subcutaneous veins and parts of the cremaster were freely visible in the denuded area. In this instance, the morbid process subsided under local treatment after a three week period of progression. The necrotic slough was gradually shed, and fresh red granulations were followed by epithelization. One month after the process had come to a standstill, the patient was completely healed. Scar formation was relatively inconspicuous. This case demonstrated clearly the marked regenerative capacity of the scrotal skin.

Histologically, biopsy material revealed a homogenous mass replacing the destroyed epidermis. The normal structure was recognizable only in the marginal areas. The whole area of demarcation showed a dense lymphocytic infiltration and thrombotic occlusion of small blood vessels.

Etiology. Fulminant gangrene of the scrotum has been attributed to various pathogenic organisms, especially to *streptococcus hemolyticus* (recently reported by Randall, Marcus) and to Milian's *bacillus gangraenae*

cutis (Milian 1917) which appears morphologically and culturally related to this B proteus group According to Nativelle its pathologic activity resembles that of B pyocyaneus. Its exact classification remains disputable Occasionally this bacillus has been found also in gangrene of other cutaneous areas The portal of entry of the infection was not mentioned in any case



FIGURE 88. Spontaneous (fulminant) gangrene of scrotum and *penis with abundant findings of b. gangraenae cutis* (Milian) (Courtesy of Dr P Balog, Cairo Egypt)

Milian s B gangraenae cutis is a short rod, with rounded ends, varying from a coccobacillary shape to a length of two to five microns, and showing an intense bipolar staining (methylene blue) It is gram negative Dark field examination reveals numerous long, very flexible ciliary processes motility is variable. The organism is aerobic, propagating rapidly under free access of air but thriving likewise, *although to a lesser degree as* an anaerobe. Culture material obtained from the oozing tissue juice reproduced gangrenous lesions in guinea pigs and rabbits, transmissible

from animal to animal with identical findings (Nativelle, Balog) Balog obtained positive agglutination tests with serum from his patient, and in oculated animals as well.

Thus, judging from the literature, two different types of bacilli seem capable of producing the same clinical form of foudroyant scrotal gangrene, namely streptococcus hemolyticus and B gangraenae cutis. Further investigation will be needed for a final etiologic definition.

Differential diagnosis must exclude diphtheria, erysipelas gangraenosum scroti and genital gangrene associated with septic thrombophlebitis of the pelvic veins. Cutaneous diphtheria can be recognized by its whitish membranaceous coverings and the presence of the diphtheria bacilli. The absence of diphtheria of the throat does not exclude cutaneous diphtheria. Also pseudodiphtheric infection must be excluded.

A special search must be made for fusospirochetosis, which may give rise to an extensive ulcus gangraenosum of the scrotal or penile region. Constant findings of hemolytic streptococci in smears and cultures, or of Milian s bacillus, corroborate the clinical diagnosis of Fournier s fulminating gangrene of the scrotum.

The differentiation of the latter disease from erysipelas gangraenosum has been previously discussed, as has also the septic gangrene secondary to thrombophlebitis of the pelvic veins.

Therapy Even as late as ten years ago, surgery with wide excisions or caustic destruction was generally indicated, when local treatment with hydrogen peroxide and local antiseptics failed to control the disease Such therapy has now been superseded by the administration of antibiotics. Penicillin cures the condition in most cases. Ebrill and O'Donaghue described the dramatic effect of penicillin (500 000 units given every four hours) in a patient with scrotal gangrene who on admission was semi conscious. Within twelve hours his condition improved, his toxic state improving rapidly The local lesion receded more slowly during the follow ing weeks under continued penicillin treatment.

In cases in which the response to penicillin appears slow or incomplete a combination with sulfonamides has been advocated (sulfadiazine) The synergetic effect of penicillin and an English product, sulfamezathine was dramatic in a patient treated by Randall (total dose of 24 million units of penicillin and 32 gm. of sulfamezathine) Marcus obtained a complete cure of fulminant spontaneous gangrene of the scrotum with much com bined treatment in a case with constant abundant findings of hemolytic streptococci. Among the newer antibiotics, terramycin or tetracycline appears to be the most promising and offers the added advantage of oral ad ministration. It may be expected to prove efficacious also in cases in which Milian s bacillus is found to be the causal agent, which according to

description. Special sections have been contributed by Katzenellenbogen (Cutaneous Leishmaniasis) and by Fasal (American Leishmaniasis). There the *therapy* has been thoroughly discussed (therapy of choice: Tartar emetic, 1 to 2 per cent solution given intravenously every third day up to about ten injections). Local treatment should support the general therapy.

Cutaneous amebiasis may develop secondary to amebic infection of the large intestine. Cutaneous infection takes place in any area of the skin exposed to the continual contact with amebic infected stools. This explains the usual location of cutaneous amebiasis in the perianal and perineal areas. A pre-existing anal fissure or fistula, or any excoriation at an exposed point of the skin, favors amebic infection (Adams). Amebic ulceration has been observed around a colostomy wound. Exceptionally

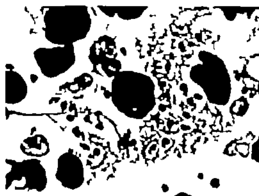


FIGURE 89. Donovan corpuscles in cutaneous Leishmaniasis (Katzenellenbogen). (Simons, *Handbook of Tropical Dermatology*. Elsevier, Amsterdam-New York, 1952, p. 338, Fig. 303.)

contact infection may occur after an occasional brief contact, as for instance in a case of Straub (cit. by Adams) who described cutaneous amebiasis of the *penis* following sodomy.

The lesions produced by continuous contact with amebic infested material have a marked tendency to expand over wide areas causing firm infiltrations, verrucous lesions and vegetating necrotic ulcerations of irregular shapes. The resistance of debilitated patients is poor and progression into the deeper tissues may be fatal. No tendency to regression has ever been noted in untreated cases.

DIFFERENTIAL DIAGNOSIS. Ulcerative lesions of cutaneous amebiasis have been mistaken for malignant tumors. Adams mentions instances of patients with cutaneous amebiasis mistakenly operated upon by radical surgical excision. Entamoeba histolytica is readily demonstrable in early cutaneous lesions.

TREATMENT of the basic intestinal infection is imperative and is effective in the majority of cases of cutaneous amebiasis. The therapy of amebic dysentery is thoroughly discussed in textbooks of Internal Medicine.



FIGURE 90 Leishmaniasis Americana, inner aspect of the thighs (Fasal) (Ibidem, p. 381 Fig. 337)

D Ulcerations of the Genitals in Acute Infectious Diseases

Both the skin and the mucous membranes of the genitals may react with the rest of the body surface to acute systemic infections. Like the oral mucosa, so also the mucous membranes of the vulva, vagina, and occasionally of the urethra, may be involved. The phenomenon of a slight discharge during the feverish period of acute infectious diseases has been discussed in Chapter 17 F

Morphologically these enanthemas of the genital mucous membranes do not differ from the types of exanthema in measles scarlet fever septicemia, etc. Eruptions of *caricella* or *cariola* when involving the vulvar mucosa, appear as small ulcers rather than as pustular efflorescences they may coalesce to larger lesions, readily exposed to secondary infection. Of particular importance are the hemorrhagic-necrotic genital lesions developing during the febrile or more frequently during the convalescent period in certain acute systemic infections.

One or more such ulcers may be found at a time when the skin shows no corresponding symptoms, and may then pose a difficult diagnostic problem. The question arises as to whether the ulcers are of hematogenous origin or causal manifestations of an exogenous infection.

Exogenous infections of the genital region are not rare in periods when the body's resistance to infections has been generally lowered. Even the presence of a positive blood culture in septic disease or in typhoid fever does not exclude a possible exogenous infection. Small furuncles or abscesses are not uncommon during convalescence.

Hemorrhagic necrotic ulcers of the vulva have been described in various forms of purpura hemorrhagica, analogous to the tonsillar or pharyngeal ulcers observed in scurvy in aleukemia hemorrhagica or in agranulocytosis Otto described a large necrotic ulcer of the vaginal mucosa in a fatal case of *agranulocytosis* autopsy revealed necrotic ulcers of the tonsils and pharynx as well as multiple ulcers of the gastric mucosa.

In *typhoid fever* genital ulcers are encountered especially during the period of convalescence Rare though they are, hematogenous ulcers of the vulva have been convincingly demonstrated, with abundant typhoid bacilli in smears, as well as in stained tissues

We were confronted with an acute irregular necrotic ulcer of the right labium minus in a woman of twenty-one years, recovering from typhoid fever The family physician had diagnosed a venereal, probably syphilitic initial lesion. However bacteriological, serological and clinical observation invalidated such a diagnosis.

Histology: According to their pathogenesis, the genital lesions under discussion vary widely in their histological aspects In ulcers of exogenous origin, the pathologic process progresses from the surface down to the deeper strata, whereas hematogenous ulcers develop from deposits of the pathogenic agents within the cutis. E. Fraenkel succeeded in demonstrating capillary bacillary thrombosis with findings of the specific organisms in the vessels as well as in perivascular inflammatory infiltrations in necrotic hematogenous ulcers, occurring in several acute infectious diseases.

As mentioned above, the differential diagnosis of genital ulcers in acute infectious diseases involves intricate problems Hematogenous lesions of the genital mucosa may present a wholly different aspect owing to superimposed infection They may masquerade as Lipschutz ulcers Vincent's ulcers, or ulcers produced by pseudodiphtherial bacilli. Brule, Hillemand and Gilbrin described vulvar ulcers of the Lipschutz type with findings of B crassus during the febrile period of typhoid fever Their origin appears doubtful, even though typhoid bacilli were demonstrated in the blood cultures.

The onset of acute infectious diseases is often accompanied by erup-

tions of herpes labialis facialis, or occasionally herpes genitalis The appearance of small, round or polycyclic erosions on the vulvar mucosa demands the consideration of such a possibility in differential diagnosis in the absence of typical herpetic lesions.

Treatment: Hematogenous genital lesions due to deposits of the specific organisms in the genital tissues, heal under treatment of the basic disease. The treatment of exogenous bacterial ulcers has been discussed in other sections of this book.

E. The Malignant Ulcer of the External Genitals

The possible presence of a malignant process must be taken into consideration in all otherwise unexplained chronic ulcers of penis, scrotum and vulva. The tendency of certain genital lesions to transform to cancerous lesions demands continual surveillance. Biopsy will be the ultimate resort *in all doubtful chronic ulcers resistant to treatment.*

The more or less pronounced, malignant potentiality of various genital lesions will be discussed in Chapter 15

Occupational malignant ulcers of the scrotum occurring in workers exposed to irritation by products of the petroleum and tar industry by paraffin or coal dust, will be detected early provided there is continuous medical control.

The complexity of the problem of tumor pathology requires a more detailed discussion of all clinical manifestations of neoplasms of the external genitals including the ulcerative stage. The reader is referred to Chapters 14 and 15.

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CHAPTER 13

DIFFUSE IRRITATIVE INFLAMMATION OF THE GLANS AND PREPUCE AND OF THE VULVA

Diabetic Balanitis and Vulvitis
References

Diffuse Irritative Inflammation of the Glans and Prepuce and of the Vulva

A great variety of inflammatory conditions, of rare infections and still unexplained lesions of the penis and vulva are described in the special sections of this book.

There remains the common form of diffuse irritative inflammation of the preputial sac, the ordinary balanitis and balanoposthitis so often encountered in the practitioner's office. As common and as trivial as they may appear these affections demand careful attention, since not infrequently they develop in association with internal disease and may thus show a tendency to persist or recur

Vulgar Balanitis and Balanoposthitis

So-called simple balanitis and balanoposthitis occur chiefly in subjects having an excessively long, tight and only partially retractable prepuce. These anatomic features favor an excessive accumulation of smegma and the development of secondary infections from the bacterial flora of the preputial sac. Sexual excesses or the mechanical irritation caused by long military marches, rides or motorcycling provoke an inflammatory reaction of the exposed area.

Itching and burning, swelling and reddening of the prepuce are accompanied by epithelial desquamation and erosions on the glans and inner sheet of the prepuce. In addition, there develops a malodorous, watery or thin purulent secretion of varying amount and bacterial content. Bacterial infection may spread to the lymphatics, producing lymphangitis or a usually slight lymphadenitis.

The micro-organisms found in the flora of the preputial sac are legion. Streptococci, staphylococci, smegma bacilli, pseudodiphtheric bacilli, vibri-

old organisms spirochetes and occasionally yeast like organisms may be found in varying proportions. Usually it is difficult to determine whether one organism or possibly several symbiotic micro-organisms, in an individ ual instance may have caused the bacterial infection.

Vulvitis acuta: A similar flora is demonstrable in the female, especially in the interlabial folds and on the clitoris but under normal condi tions, usually outnumbered by Doederlein bacilli. It is often difficult to determine the specific pathogenic role of any one or more of these organ-



FIGURE 91 Abscess with symptomatic edema of the vulva, forming beneath the clitoris. Origin unknown, possibly due to infection by scratching. Note edema of the vulva. (Dermat. Clinic, Frankfurt, Prof. Dr O Gans.)

isms in an individual case. Warmth, moisture and traumatic irritation are predisposing factors, which act by softening and loosening the epithelial layer Erosions readily develop and render favorable conditions for bacterial infection. The anatomical structure of the vulvar tissues promote the development of excessive edema.

Irritative diffuse inflammations of the vulva usually proceed from the folds around the clitoris or the interlabial folds i.e., from areas less acces sible to air and thus favoring anaerobic growth.

Of particular importance is the irritative inflammation of the vulva caused by intestinal worms. Acute and subacute vulvitis in children demand careful examination for *oxyuriasis*. Numerous worms may reach the vulva from the anal region causing itching, scratching and erosions.

Differential Diagnosis

Unless phimosis hampers full retraction of the prepuce, the diagnosis of diffuse irritative balanitis is simple. Infiltrations of the preputial sac palpable through the phimotic prepuce may suggest venereal infection. Retrogression or surgical treatment of the concurrent phimosis may prove these lesions to be purely inflammatory

The differential diagnosis includes herpetic inflammation balanitis *erosiva circinata and balanitis diabetica. In vulgar balanitis the erosions* of the glans and prepuce are indistinct and varying in extent in contrast to the minute distinct erosions in herpes progenitalis and to the larger round ish or polycyclic lesions in balanitis erosiva circinata. Diffuse inflammatory balanitis in its common form does not show any tendency to ulcer forma tion like that seen in diabetic balanitis or to necrosis, as observed in balani tis erosiva circinata and gangraenosa moreover fusospirochetosis is absent.

The differentiation and management of various forms of acute balani tis and vulvitis are discussed in connection with vulvitis circinata et gan graenosa in Chapter 12.

*Common balanitis and balanoposthitis run a shorter course than bal*anitis and vulvitis diabetica and respond promptly to *antiphlogistic and antiseptic treatment* As a rule phimosis acquired during common balanitis disappears under this therapy Dorsal incision or circumcision are seldom necessary except in patients with a pre-existing congenital phimosis

In any case of balanoposthitis that shows stubborn resistance to proper local treatment, or a tendency to relapse, a careful examination of the urinary and blood sugar is imperative.

Diabetic Balanoposthitis and Vulvitis

Stout persons and especially stout diabetics are predisposed to inflammations of the preputial sac or to vulvitis. In diabetic patients this predisposition is chiefly due to disturbances in cellular nutrition inadequate carbohydrate and fat metabolism or to vitamin deficiency after high carbohydrate diet (Parks and Martin) Moreover the glucose containing urine favors the propagation of bacteria and mycotic organisms (monilia albicans) Monilial balanitis and vulvitis are discussed in Chapter 2.

Elaborate studies dealing especially with the symptomatology and pathogenesis of balanitis diabetica have been published (Englisch, Scherber *et al.*) In this condition, the glans penis loses its normal smooth appearance showing increasing redness and a velvety aspect. The margin of the urethral meatus is also swollen and reddened, the prepuce being edematous and swollen, with its distal portion rigid, thickened and immovable

Attempts to retract the prepuce may produce fissuration. The erosions of the glans and prepuce change into roundish ulcers covered with a viscid, fetid, and later more purulent secretion.

The secretion contains numerous bacteria and characteristically often mycotic filaments and spores belonging predominantly to fungi of the candida group The question as to the actual pathogenic or merely inciden tal role of these mycotic elements in the individual case must be left open in many instances

Diabetic balanitis is found in only a relatively small percentage of all diabetics. According to reported statistics the incidence is about 7 per cent.

Differential Diagnosis

In patients with a positive diabetic history the diagnosis of balanoposthitis diabetica is self suggested. Otherwise a whole host of infectious inflammations and ulcers will have to be excluded. The demonstration of a fusospirochetosis will suggest balanitis erosiva circinata and gangraenosa. Constant or predominant bacterial findings may point to a possibly specific secondary infection with streptococci, pseudodiphtherial bacilli, etc. Such findings would not, of course, exclude the presence of a basic diabetes

As previously emphasized, urine and blood examinations are indispen sable for the diagnosis of excessive or recurrent balanoposthitis. Urinary findings may be negative at first, while the blood sugar level will indicate latent diabetes. Following an initially negative result of both of those laboratory tests, repeated tests must be made at intervals.

Vulvitis diabetica presents symptoms analogous to those seen in dia betic balanitis There is a more or less intense reddening and inflammatory infiltration of the labia majora, associated with a velvety swelling of the mucous membranes of the vulva. Irregular superficial erosions may de velop and may disappear spontaneously to be followed by new lesions. The loosened epithelium is predisposed to bacterial infection resulting in more conspicuous yellowish gray ulcers. A slight to moderate discharge and as a rule, an annoying pruritis accompany the condition. The presence of mycotic organisms, especially of yeast or yeast like fungi so common as saprophytes of vulva and vagina, gives rise to vulvar moniliasis (see Chapter 2) Insulin and dietary control are paramount in the management of vulvitis diabetica, in addition, local therapy with mild disinfectants (dressings or ointments) will suffice to cure this affection Intertrigo caused by obesity is a frequent complication of diabetic vulvitis

Balanitides caused by an *excessive excretion of urates* in *gouty* pa tients are usually mild as compared with balanitis in diabetics. Burning and itching may be more intense when the uric acid or phosphate deposits

accumulate in the presence of partial or complete phimosis. However subjective symptoms may be irrelevant, even when stagnation of urine has led to the formation of preputial concretions The latter may remain unnoticed in the phimotic preputial sac for a long time.

Treatment

The management of balanitis diabetica must be focused upon control of the basic disease Constant vigilance dietary regulations and insulin administration will accelerate healing under supportive local therapy and may incidentally prevent recurrence The local treatment will depend upon the bacterial findings in smears from ulcers of the glans or prepuce. The local treatment for bacterial ulcers of the penis and vulva has been described in various chapters In administering antibiotics to diabetics, a cautious selection of the compound careful dosage and continuous observation of the patient are required.

Inflammatory Phimosis—Preputial Stones

Inflammatory phimosis may be caused by (1) infectious lesions of the glans and prepuce, (2) neoplastic growth, or (3) by foreign bodies obstructing the preputial sac, such as inspissated calcifying smegma masses or preputial stones.

We have repeatedly emphasized the diagnostic difficulties encountered in prompt identification of underlying causal lesions in the presence of complicating congenital or acquired phimosis. An exact diagnosis may be impossible also when the prepuce is only partially retractable since the coronary sulcus and its vicinity constitute sites of predilection for infectious lesions.

Management of this complication will require a thorough familiarity with all internal and external factors that may provoke an inflammatory reaction of the glans and prepuce

The presence of initial manifestations of syphilis or of malignant growth must be excluded or given immediate attention. The external palpation of an inflammatory infiltrated prepuce will not furnish a reliable procedure for the detection of chancre hidden under the covering prepuce spirochetes are rarely demonstrable among the numerous micro-organisms in the purulent discharge of inflammatory phimosis Valuable time may be wasted by adoption of an expectant attitude in doubtful cases. Dorsal incision, if not circumcision, is strongly advised to lay bare the whole involved area.

An expectant attitude does seem justifiable however in phimosis developing from diffuse irritative inflammations such as the vulgar forms of

balanitis and balanoposthitis. Such an attitude is likewise permissible in the management of *uncomplicated congenital phimosis in infants* The foreskin of the newborn infant is normally non-retractable Complete retractability develops spontaneously but has never been reported earlier than six months after birth and may not be achieved before the fifth year of life (Gairdner)

It would exceed the purpose of this book to describe the surgical technic employed for the treatment of congenital or acquired phimosis. This aspect will be found thoroughly described in surgical and urologic text books.

The *preventive* value of circumcision in infants especially of ritual circumcision of the newborn, is discussed in connection with carcinoma penis.

Preputial stones These may form in an obstructed preputial sac due to the excessive accumulation and decomposition of the smegma masses impregnated with calcium salts from the stagnant urine. Microscopically these masses consist of epithelial cells cholesterol crystals calcium particles and decayed bacteria. Or concretions may form directly from deposits of urates, calcium phosphate and ammonio-magnesium phosphate excreted with the urine. These calculi are of light weight and usually of a plaster like, friable consistency Other concretions may form around true bladder stones or kidney stones wedged between the glans and prepuce. Preputial stones with sharp edges may cause pressure necrosis and ulcers, and, occasionally may perforate the prepuce. Spontaneous elimination of such massive stones is uncommon Preputial stones develop very slowly and may remain unnoticed until inflammation causes pain and phimosis. Dorsal incision of the prepuce suffices for removal of these calculi.

For instances of *paraphimosis* frequently the result of futile attempts of the patient to retract a partially immovable and swollen prepuce, the causal lesions can usually be recognized in the majority of cases, even before surgical dissection of the strangulating preputial ring.

Trauma, sexual intercourse or a possible infection have been supposed to be causative factors in an otherwise unexplained formation of *thrombosis of the vena dorsalis penis* This vascular affection was strictly confined to the dorsal vein of the penis in all instances reported. Muschat (1941) described this lesion as a well defined hard mass extending in its entirety to the base of the penis. No pain was noted, no redness was present. Kimbrough and Morse (1951) studied the histological picture encountered in sections from the extirpated cord like induration. There was an obliterating thrombus containing slit-like intravascular spaces which indicated recanalization There will be little difficulty to distinguish this condition from diffuse inflammatory infiltrations of the penis.

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CHAPTER 14

PROGRESSIVE SCLEROTIC ATROPHIC PROCESSES OF PENIS AND VULVA

Balanitis Xerotica Obliterans, Kraurosis Glandis et Praeputii and Lichen Sclerosus et Atrophicans
Leucoplakia (Leucokeratosis) Penis
Kraurosis and Leucoplakia Vulvae
References

Balanitis Xerotica Obliterans, Kraurosis Glandis et Praeputu and Lichen Sclerosus et Atrophicans

Balanitis xerotica obliterans and kraurosis glandis et praeputii are closelv related affections. A progressive sclerotic, atrophic process is characteristic of both conditions. Stühmer in his first description (1928) uses the term "balanitis xerotica obliterans (post-operationem) to describe a case in which a faulty operation upon a congenital phimosis with chronic inflammation of the glans and prepuce preceded the shrinking process. Later this condition was observed also in cases without any history of previous operation. In every case, however a chronic, relapsing balanoposthitis was recorded. Chronic inflammation gradually leads to sclerosis atrophy and adhesions between prepuce and glans. The preputial sac is obliterated and constriction of the urethral meatus causes painful micturition and dysuria.

The condition is not very rare In addition to the six cases reported by Stühmer and other scattered case reports Freeman and Laymon reported eighteen cases in 1941 and six other cases in 1944. The patients were all of middle or advanced age. Transformation into carcinoma has been described by Stühmer and by Fruhwald

Kraurosis glandis et praeputii was first described by Delbanco (1908) He did not believe that chronic balanitis must necessarily precede the development of kraurosis. Narrowing of the prepuce and stenosis of the urethra orifice are products of a particular morbid process According to Delbanco the atrophic areas are more distinct in kraurosis penis they contrast markedly with the normal skin Occasionally the shaft of the penis is involved. He observed paresthesia and violent itching in eight patients and considered the affection as a disease entity having no connection with the clinically similar kraurosis of the vulva.

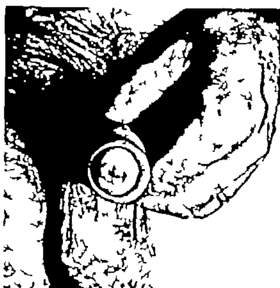


FIGURE 92. Balanitis xerotica obliterans.



FIGURE 92a. Same patient. Flattening of the epithelium, marked atrophy of the upper corium.



FIGURE 93. Balanitis xerotica bliterans, same patient.

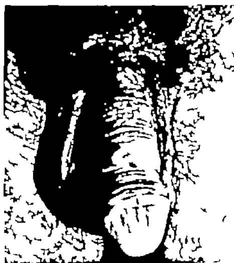


FIGURE 94. The same patient as in Figs. 92 and 93. Note atrophic changes of the glans.



FIGURE 95 Same patient. Note depigmentation and atrophic changes of prepuce.

Histology

Flattening of the malpighian stratum extensive edema of the connective tissue, changes or loss of the elastic fibers and perivascular infiltration with plasma cells (Delbanco) In accordance with other observers, Delbanco considered the vascular net of the cutis as the starting point of the pathologic process.

Today balanitis xerotica obliterans and Delbanco's kraurosis glandis et praeputii are considered as identical. The opinion prevails that both affections are closely related to lichen sclerosus et atrophicans Special studies by Laymon (1951) and by Wallace and Nomland (1948) support the classification of these conditions as variants of lichen sclerosus et atrophicans.

According to Laymon, *lichen sclerosus et atrophicans*, in its genital location in the male appears in two forms (1) as isolated papules on the shaft of the penis, and (2) as a constricting band about the prepuce with circumscribed or coalescing white atrophic plaques on the glans and prepuce and stenosis of the urethral orifice. Both forms may appear singly or combined. *They may or may not be associated with symptoms of lichen* sclerosus et atrophicans elsewhere on the body i.e., with the typical whitish papules showing keratotic plugs and cells in lesions undergoing *involution Laymon missed this combination in eighteen cases, but later* together with Freeman, observed four patients with balanitis xerotica obliterans of the glans and prepuce associated with white papules of lichen sclerosus et atrophicans on the shaft of the penis. F Becker *in another* case noted unmistakable papules of lichen sclerosus et atrophicans on the shaft and the scrotum, in addition to lesions on the clavicular and scapular skin combined with balanitis xerotica obliterans. Degos, Ancelin and

Legrain (1951) found sclerotic atrophic changes of the glans penis in association with clinically and histologically typical lesions of lichen *planus* on the prepuce in a forty-eight year old man.

Lichen sclerosus et atrophicans of the genitals occurs also in females. In twenty out of thirty-eight women observed by Montgomery and Hill, vulvar and perianal symptoms were combined with lichen sclerosus et atrophicans of other regions. In only six out of forty-six instances, was the affection limited to the anogenital region. Laymon found genital lichen

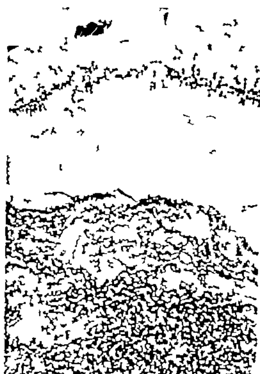


FIGURE 96 Balanitis xerotica obliterans, histological picture acanthosis, papillary and subpapillary edema, loss of elastic fibers, lymphocytic infiltration. Section taken from the glans near the meatus. (Courtesy of Prof. Dr. A. Midana, Torino, Italy.)

sclerosus et atrophicans in three girls under six years of age: such incidences in childhood are not rare. Pruritus is absent or moderate in this condition.

The *histological* features of balanitis xerotica obliterans and lichen sclerosus et atrophicans of the genitals, are essentially identical. Typical of the genital location is the presence of a band of homogenization in the upper cutis, probably developing from a subepithelial edema with flattening of the papillary bodies (Laymon). Beneath this zone there is inflammatory infiltration of varying intensity.

Elaborate histological studies have been presented by Frishwasser and Finkle, Midana, Czonka, Laymon.

The *etiology* of balanitis xerotica obliterans, kraurosis glandis et praeputii and lichen sclerosus et atrophicans is obscure There is no definite proof that a deficiency of sex hormones like that noted in kraurosis vulvae, plays any significant role in the pathogenesis of these genital affections.

Differential Diagnosis

These genital affections must be distinguished from other nonvenereal diseases of the genitals such as localized *scleroderma* and *lichen planus* Scherber described an isolated patch of scleroderma of the penis in a man of fifty-two years. The foremost part of the prepuce presented a sharply demarcated, shiny zone of a yellowish white color which revealed an increased density and rigidity on palpation A small red area around the lesion enhanced the contrast with the normal skin The sclerotic process extended to the adjacent inner lamina of the prepuce. Histologically the features characteristic of scleroderma were demonstrable, namely a flattening of the papillary body sclerosis of the connective tissue, and intense inflammatory infiltration of the basal layer of the epidermis.

Differentiation from lichen planus is simple in the presence of lichen planus papules elsewhere on the body The initial whitish color typical of *lichen sclerosus et atrophicans differs markedly from the appearance of a* lichen planus nodule. The differentiation from kraurosis vulvae will be discussed in the following section.

Therapy

There is no specific therapy for these conditions of unknown etiology Surgical removal of a phimotic prepuce with chronic, relapsing balanoposthitis *is always indicated. Reports on the effectiveness of estrogen therapy* in lichen sclerosus et atrophicans of the genitals are scarce and do not allow definite therapeutic conclusions. One of us has noted an apparent regression in a case of balanitis xerotica obliterans, observed for a period of six months while using a topical application of a lotion containing two and one-half per cent hydrocortisone acetate

Leucoplakia (Leucokeratosis) Penis, Kraurosis and Leucoplakia Vulvae

Leucoplakia glandis et praeputii (von Franqué or Fuchs) [*Leucokeratosis* (Kraus, 1907)] is usually preceded by a chronic relapsing balanoposthitis due to congenital phimosis. Clinically and histologically this condition resembles leucoplakia of the oral mucosa and the tongue The penile affection is likewise characterized by the formation of one or more circumscribed, slightly elevated, milky or bluish white later shiny silvery patches, produced by epithelial proliferation and keratinization. Similar

plaques may be seen near the meatus, occasionally extending to the adjacent urethral mucosa. Erosions and ulcer formation are not uncommon Adhesions between the inner preputial lamina and the glans occur fissures may develop from the trauma of intercourse An intense itching accompanies the condition.



FIGURE 97 Leucokeratosis of glans penis. (Courtesy of Dr T Benedek, *Chicago*)



FIGURE 98. Same patient as Fig 97 Inter-and subpapillary cell infiltration, dilatation of small blood vessels.

Occasionally leucoplakia penis has been found associated with atrophic changes similar to those in kraurosis glandis et praeputii What, then could be more suggestive than a comparison of leucoplakia penis with kraurosis and leucoplakia vulvae? The malignant potentiality of leucoplakia vulvae *is also inherent to leucoplakia penis. Statistics* concerning the fre-

quency of malignant transformation however are lacking in penile leucoplakia.

Histologically the picture is identical with that of buccal leucoplakia. Kraus, Fuchs Benedek, Dick, *et al.* described acanthosis, spongiosis, hyper and parakeratosis edema, circumscribed inflammatory infiltration and loss



FIGURE 99 Leucoplakia penis associated with chronic balanitis. (Dermat. Clinic of the Freie Universitat, West Berlin, Prof Dr E. Langer)

of elastic fibers. The epithelial changes dominate the microscopical appearance.

The *etiology* is obscure

Therapy

Leucoplakia of the male genitals calls for continuous observation and vigilance Biopsy is imperative. Phimosis should be eliminated surgically If malignant transformation is suspected, plaques remaining on the glands should be destroyed by electrosurgical methods. Once malignancy is evident radical surgical intervention including the extirpation of regional glands is indispensable.

The recently suggested treatment of leucoplakia with *Vitamin A* is of purely hypothetical interest. Authors assuming its possible efficacy have prescribed 250 000 units to 500 000 units of Vitamin A per day by mouth, supplemented by 50 000 units intramuscularly twice a week. Hyams and Bloom noted marked relief from itching following such treatment in fourteen of eighteen patients.

Kraurosis and Leucoplakia Vulvae

The clinical and histological symptomatology of kraurosis vulvae is described in full detail in gynecological textbooks and monographs

Kraurosis vulvae develops in women after the menopause, and occasionally in younger women following extirpation of the ovaries. As noted by Baird, kraurosis vulvae is essentially an exaggeration of the normal post menopausal atrophy The labia majora and minora and the clitoris diminish in size and finally disappear Contraction of the introitus favors the development of fissures with sexual intercourse and usually causes dyspareunia. The mucosa becomes dry and smooth the involved areas are of a white or



FIGURE 100 Leucokeratosis of the glans penis, developing near the meatus, note semicircular thickening. (Freie Universitat, West Berlin, Prof. Dr E. Langer)

yellowish color The skin of the vulva is thinned and discolored containing pigmentary deposits The pubic hair becomes sparse As a rule, an intolerable pruritus accompanies the tormenting condition and pain on micturition is common *scratching may cause chronic intertriginous dermatitis as* seen in Fig 101.

The combination of kraurosis vulvae with leucoplakia is frequent, but kraurosis vulvae is not necessarily associated with leucoplakia. Present opinions seem to agree that this coincidence should not be interpreted as indicating a common etiology The two conditions should be differentiated. Leucoplakia vulvae may occur independent of kraurosis as a spontaneous genital condition similar to leucoplakia buccalis The coincidence of kraurosis and leucoplakia vulvae however has been frequently observed. Goldberger estimated that about 50 per cent of all cases of kraurosis vulvae are associated with leucoplakia.



FIGURE 101. Chronic pseudomembranous intertriginous dermatitis in kraurosis vulvae. (Dermat. Clinic, Frankfurt, Prof Dr O Gans.)



FIGURE 102. Chronic and trophic leucoplakic vulvitis.

Malignant transformation of leucoplakia vulvae occurs frequently According to Goldberger about half of all combined cases should be expected to undergo carcinomatous changes. Other statistics indicate that at least 50 per cent of all cases of carcinoma vulvae are derived from leucoplakia (Taussig thirty nine of sixty four cases) There is some doubt that kraurosis vulvae itself can undergo malignant transformation in the absence of

leucoplakia. Opinions differ In combined cases it may be assumed that leucoplakia is the starting point of the cancerous growth

Histologic changes in kraurosis vulvae thinning of the whole epithelial layer flattening of the papillary bodies marked keratinization, loss of the elastic tissue, which is replaced by a homogenous layer containing little collagen and without associated inflammatory infiltration. Edema and dilatation of blood vessels are more or less marked.

The *etiology* of both kraurosis and leucoplakia vulvae is still under discussion Kraurosis vulvae appearing after the menopause or after removal of the ovaries has been generally attributed to a deficiency of estrogenic hormones. The tentative theory of a possible role of a Vitamin A deficiency in the pathogenesis of leucoplakia has been previously discussed.

Differential Diagnosis

As above mentioned the pathologic processes in kraurosis and leucoplakia differ essentially In other words, leucoplakia vulvae should not be considered as an evolutionary stage in the pathogenesis of kraurosis. The pathologic process is atrophic from the beginning in kraurosis, while in leucoplakia vulvae it is of the hypertrophic hyperplastic type. We believe that the formation of more or less circumscribed leucoplakia does not fit to the pattern of the diffuse mucocutaneous atrophic process in kraurosis vulvae

The differential diagnosis of kraurosis vulvae from lichen sclerosus et atrophicans has been in the limelight for several years Laymon recently suggested a possible close relation of kraurosis vulvae to lichen sclerosus et atrophicans "It would seem that there is more evidence in favor of classifying kraurosis vulvae as a type of lichen sclerosus et atrophicans affecting the female genitals than there is in classifying it as a distinct entity "

This suggestion is in harmony with the modern tendency to integrate clinically and histologically similar conditions of obscure origin. This *creation of new disease entities supplies material for promoting discussion* and for further etiological research.

The striking clinical and histological similarities of both conditions under discussion have been emphasized previously Proportionally some of the differences appear of minor importance lichen sclerosus et atrophicans of the genitals is often associated with characteristic lesions on other parts of the body and especially with perianal lesions. Montgomery believes that the marked changes of the deeper blood vessels encountered in kraurosis vulvae are lacking in lichen sclerosus et atrophicans Ebert, in a discussion of Laymon's paper emphasized the apparent predilection of lichen sclerosus et atrophicans for the extremities of life," namely

during puberty or in women after the menopause. Difference of opinion will continue as long as there is no distinct proof of a common etiology

It is, of course highly important that the secondary changes produced by rubbing and scratching in neurodermatitis be differentiated from leucoplakia. Local relief with 2½ per cent hydrocortisone ointment may cause prompt disappearance of such whitish areas and so make unnecessary the consideration of radical surgery

Therapy

Estrogen treatment, orally parenterally or by local application in ointment form should be tried in every case of kraurosis vulvae Response, however may vary or be lacking Reports indicate that at least itching can be controlled by estrogen treatment. G L. Buxton recommends an ointment, consisting of a hydrated lanolin base with 10 mg. of diethylstilbestrol per 30 gm. of ointment. Thirty gm. of this ointment should be applied daily for one week. If a response is to be expected, it will be evident within this period. A higher dosage or a protracted application may cause vaginal bleeding owing to an actual proliferation of the atrophic endometrium.

Roentgen therapy is widely used to control itching of the vulvae for a more or less extended period. However in an atrophic condition such as kraurosis vulvae roentgenotherapy should be used with the utmost caution if at all.

In extensive kraurosis vulvae with unbearable pruritus, vulvectomy has been widely recommended. However scars remaining after operation may shrink again and cause a relapse of the clinical symptoms, and in particular of pruritus.

It is important that leucoplakia vulvae be destroyed before the development of carcinomatous changes. Some sudden onset and early metastasis have been influential in prejudicing many gynecologists to such a radical procedure as vulvectomy even in early cases of leucoplakia vulvae When small areas are involved, biopsy followed by destruction by electrocoagulation, gives a satisfactory result. One should not hesitate to resort to frequent biopsy for the purpose of ruling out malignant degeneration of these lesions.

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CHAPTER 15

NEOPLASMS OF THE EXTERNAL GENITALS

A. Benign Cutaneous Neoplasms
B. Malignant Neoplasms
References

A. Benign Cutaneous Neoplasms

Introduction
Fibromas
Lipomas
Leiomyomas
Neurofibromas
Sweat Gland Tumors
Nevus Syringo-cystadenomatosus Papilliferum
Lymphangiomas
Hemangiomas
Hereditary Hemorrhagic Telangiectasia
Angiokeratoma Scroti
Epithelial Cysts
Follicular (Retention) Cysts
Myxomatous Cysts
Supernumerary Mammary Gland Tissue
Pigmented Nevi

Introduction

The lesions to be discussed in this chapter are either cutaneous manifestations of malformations or in the majority of instances, true neoplasms. In other words, they represent either casual congenital anomalies of the skin or structures of neviform character primarily preformed in the germ plasm and often appearing as hereditary phenomena. Some of these lesions have a particular tendency to degenerate or to grow and occasionally to undergo malignant transformation.

Benign neoplasms of the external genitals become manifest during infancy or adolescence. Especially in females, benign neoplasms of the genitals may escape unnoticed for years due to the complete absence of pain. Frequently such tumors are detected accidentally during a gynecological examination.

The most common of these lesions are histiocytomas i.e. simple or mixed fibromas, neurofibromas, leiomyomas, lipomas, lymphangiomas and hemangiomas. Genital neoplasms of epithelial origin appear usually as papillomas epidermoid cysts or tumors of the sweat glands. Pigmented nevi are common findings in the genital region of both sexes.

In harmony with the purpose of this book, the following selection has been made with regard to the diagnostic and practical importance of the

lesions to be discussed, rather than to their histopathologic peculiarities and their classification. The definition and classification of many of these structures are still subject to changes with further advances in our limited knowledge of their origin. Their histological features entail intricate problems. Frequently the proliferative process is not restricted to one tissue element, but proceeds simultaneously from two or more dermal structures. Textbooks of pathology and surgery and recent reviews on tumors of the skin will supply all information on the histopathologic details and their present interpretation The symptomatology and significance of these lesions as *genital* affections constitute the major subject of the following presentation.

Fibromas

Fibromas of the labia majora appear as hardly discernible firm smooth nodules beneath the epidermis. They exhibit a marked growth tendency and like the female genital tissues in general, are subjected to



FIGURE 103. Fibroma of perineum (fibroma pendulum)

marked variations in blood supply during menstrual periods and during pregnancy (Weinshel) This fact may explain their occasional excessive increase in size in adult women. These tumors gain gradually in weight and "stretching out the tissue to which they are attached to form a broad thin band, become pedunculated (fibroma pendulum) Hanging down between the thighs they are exposed to friction in walking to irritation by sweat and urine and consequently to inflammation erosion and ulceration. After they have been present for a long time, fibromatous tumors are inclined to undergo cystic or myxomatous degeneration. Unless they are removed in time, they may undergo malignant transformation.

In the male subepidermal fibromas are found especially on the scrotum.

Lipomas

Lipomas of the vulva and the mons pubis grow very slowly but may occasionally reach the size of an egg or a man's fist. They remain painless, and persist as prominent, smooth tumors. Lipomas of excessive growth tendency have been described, leading to enormous enlargement of the scrotum. Gussew described a *giant fibrolipoma of the scrotum* in a sixty five-year-old man. The penis was entirely hidden within the tumor masses. The extirpated neoplasm measuring 104 to 90 cm in its frontal and sagittal



Figure 104. Fibrolipoma of the right labium majus in an 8-year-old child.

diameters had a weight of 20 kg Lipomas and likewise the rare *chondromas* and *osteomas* of the scrotum, are often adherent to the tunica vaginalis and consequently are difficult to extirpate.

Leiomyomas

Leiomyomas of the genitals are rare Just as on the face, neck, arms and thighs, so also on the skin of the scrotum or the labia majora, they may appear as single, or occasionally multiple, firm round or oval nodules, varying in color from pink to deep red or brownish Their size varies from that of a pinhead to that of a pea. Leiomyomas when fully developed, are painful and tender to the touch The pains may be severe at times, due to concentration of their muscular constituents, which are derived from the arrectores pilorum or from the adventitia of the vascular walls.

Neurofibromas

Neurofibromas occur in connection with but also independent of Recklinghausen's neurofibromatosis as single or multiple tumors of the vulva, penis and scrotum.



FIGURE 105 Vulvar hypertrophy in cutaneous neurofibromatosis (von Recklinghausen) (Dermat Clinic, Univ of Naples, Prof Dr M Monacelli.)

Sweat Gland Tumors

Sweat gland tumors occasionally occur in the genital region prevailingly in females. The great majority of these tumors are benign However malignancy may occur As to the degree of their malignant potentiality opinions differ An estimate of 25 per cent (Novak and Stevenson 1945) may appear rather high as compared with other statistics however their statements are based on a careful study of the literature and fifteen of their own observations

In the majority of cases sweat gland tumors of the genitals have been found located on the labia majora and the surrounding skin district, rarely in the labia minora. They occur as single lesions, or less frequently as multiple well circumscribed, small solid or cystic tumors of various size (up to 1.5 cm. in diameter) Heredity has been demonstrated for several forms of sweat gland tumors

The classification and histological definition of these neoplasms are still controversial. They are hyper or metaplastic structures derived from eccrine or less frequently from apocrine sweat glands. Hidradenomas show a characteristic lining covered by a double epithelial layer Many of these lesions are more or less cystic. The reader is referred to recent studies of Danforth (1949) and of Novak and Stevenson (1945)

Nevus Syringo-cystadenomatosus Papilliformis

Special attention has been directed to a papillary form of hidradenoma described in the dermatological literature as "*nevus syringo-cystadenomatosus papilliformis*" or "*hidradenoma papilliforme*." The inguinal-genital region are favorite sites of this type of hidradenoma (Werther, Friboes, Beerman). This neoplasm consists of single or multiple, sometimes grouped, firm reddish papules of about the size of millet seeds. Such a papule may grow slightly and then remain the same size. When fully developed, the nodules are umbilicated. Tiny vesicle-like inclusions may be seen. Clinically

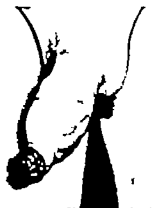


FIGURE 106. Naevus verrucosus (systemat.) in a 2-year-old child. (Dermat. Clinic, Frankfurt, Prof. Dr. O. Gans.)

such lesions may simulate molluscum contagiosum (Beerman). Kreibich (cited by Beerman) described papillary growth on the surface of such a nodule. The histology has been described by Werther, Friboes, Gans, Stokes, *et al.*

Lymphangiomas

Lymphangiomas of the genitals, rare in both sexes, occur either as lymphangiectasis or as the cavernous "*lymphangioma circumscriptum*." The latter type develops from an aggregate of deep-seated lymphangiectatic structures. Translucent vesicles appear scattered over certain areas or arranged in groups. These lesions have been earmarked as "frog spawn-like" eruptions. Occasionally the lymph vesicles have a reddish hue owing to small hemorrhages. When punctured or rupturing, they exude a lymphatic fluid that coagulates into thin crusts. Massive forms of lymphangioma have been observed causing considerable enlargements of the labia majora. When involving the scrotum lymphangioma circumscriptum manifests itself as an eruption of vesicles varying in size from that of a millet

seed to that of a bean. Rarely vesicles are found on the shaft of the penis or in the inguinal folds

Hemangiomas

All varieties of *hemangioma* both superficial, telangiectatic and deep, cavernous forms as well, involve the genital region. Single and multiple hemangiomas occur on the scrotum and penis (seldom on the glans) on the labia majora and minora, the posterior commissure or the clitoris

Hemangiomas of the genitals may include the mucosa and may be associated with vaginal and rectal hemangiomas R. and A. Bensaude observed two cases of mucocutaneous hemangioma involving the scrotum,

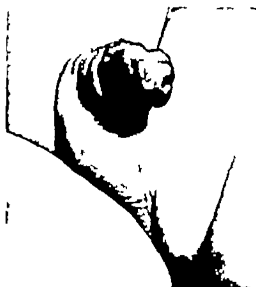


FIGURE 107 Cavernous hemangioma, glans penis.

penis and rectal mucosa. In one of the patients, a large cavernous angiomatous tumor of the rectal mucosa was combined with warty prominent formations at the root of the shaft of the penis Periodical anal hemorrhages necessitated hospitalization. The highly anemic patient succumbed following a severe uncontrollable rectal hemorrhage.

Hereditary Hemorrhagic Telangiectasis

The genital region is one of the sites of predilection in *hereditary hemorrhagic telangiectasis* This is a well recognized, but rare disease described by Rendu (1896) and Osler (1901) and appears to be transmitted from one generation to another one about equally by males and females. In some families, the condition could be traced back through six generations

Hereditary hemorrhagic telangiectasis is characterized by (1) the presence of mucocutaneous telangiectases in a typical distribution (2) the

involvement of internal organs (cavernous angioma or plexiform telangiectases of the lungs the visceral or urinary organs) (3) a marked tendency toward hemorrhages (epistaxis hemoptysis hematuria) (4) a normal blood picture, except for a more or less severe, secondary anemia, resulting from repeated hemorrhages and (5) an hereditary or familial incidence. Cases of fatal hemorrhage from pulmonary or intestinal lesions have been reported.

The mucocutaneous lesions consist of pin-point angiomas, spider angiomas and predominantly nodular telangiectases of a purple color They are most frequently found on the face, the tongue, the oral and nasal



FIGURE 108. Hereditary hemorrhagic telangiectasis of scrotum. (Courtesy of Dr William N New)

mucosae, occasionally involving the conjunctiva, and, frequently the *genitals*, in particular the *scrotum* which may be covered by a plexiform convolution of dark blue nodular telangiectases. Hemorrhages occur spontaneously or following trifling injury (Fig. 108)

Usually this vascular defect manifests itself by recurrent epistaxis, beginning in childhood, or more frequently after puberty Cutaneous lesions may develop or attract attention later occasionally as late as the third decade of life.

The tendency to hemorrhages in hereditary telangiectasis is due to an extraordinary fragility of the walls of the dilated vessels. *Histological* studies have revealed an almost total lack of elastic and muscular elements in the vascular walls as compared with the normal structures in uninvolved areas.

The *treatment* of mucocutaneous telangiectasis is the same that is generally applied for angiomas In cases with severe epistaxis and hemorrhage from the internal organs administration of rutin over a long period has been recommended (Rumball Cope and Grover) Rumball obtained prompt response to rutin in doses of 20 to 40 mg. thrice daily in a patient who suffered from epistaxis gastric or rectal hemorrhages about every two months.

The *dermatologist will find detailed information on this condition,* especially in Cockayne's book on inherited anomalies of the skin (1933) or in Garland and Anning's genetic and bibliographic study (1950)

Angiokeratoma Scroti

Angiokeratoma scroti is the term used to designate a rare scrotal affection which resembles but possibly is not identical with Mibelli's



FIGURE 109 Angiokeratoma of the scrotum, Mibelli's type (Dermat Clinic, Univ of Naples, Prof Dr M Monacelli.)

angiokeratoma. The scrotal angiokeratoma, as seen in Figure 109 consists of circumscribed pinhead to pea sized dark blue compressible nodules *showing a smooth or hyperkeratotic surface It occurs usually in men* of forty to fifty years of age. The histological picture presents telangiectatic or varix like vascular spaces of the uppermost, occasionally of the deeper veins of the corium, the covering epidermis being thinned or slightly to moderately hyperkeratotic. A possible neviform nature has been suggested by Fabry

Epidermoid Cysts

Of the great variety of *congenital* epithelial cysts it is chiefly *epidermoid cysts* that are observed on the genitals These are neviform structures

containing partly sebaceous, partly epithelial elements They form single or multiple subcutaneous tumors of various size. Epidermoid cysts should not be confused with so-called *dermoid cysts*, which are also occasionally located in the genital region and, if so are almost always situated on or near the perineogenital raphe. They contain a mixture of most diversified tissue elements, including almost all epidermal structures, glandular appendages, hair and calcified matter They are lined with a stratified layer of squamous cells Dermoid cysts are individual congenital anomalies they are not hereditary like the epidermoid cysts, which have been observed as familial neviform formations through several generations (W Siemens) Epidermoid cysts are generally considered as benign neoplasms, analogous to epithelial and sebaceous cysts.

Epithelial Cysts

Epithelial cysts, due to traumatic implantation of squamous epithelial cells, or to prenatal epithelial intussusception are rare in the genital region. Similarly the epidermoid cysts have been interpreted as being derived from epidermal invagination. Their histological differentiation from *follicular* cysts may prove difficult.

Follicular Cysts

Follicular (retention) cysts may be found on any part of the skin. In the genital area, they appear as one or more discrete firm, spheroid tumors of pea to cherry-size. They are encapsulated, presenting a fibrous lining with an epithelial layer Glass pressure will reveal their yellowish contents. They are filled with a grit-like mass frequently intermingled with calcified matter Occasionally such a tumor may present a less solid consistency owing to fluctuation and when punctured yields an oily fluid. Multiple follicular cysts are found especially on the scrotum In the earlier literature, we encounter this lesion under the now obsolete term atheroma, which was commonly applied to retention cysts, epidermoid cysts and xanthomatous forms as well. Beerman believes that multiple follicular cysts are in fact multiple sebaceous cysts.

The scrotal skin appears to be particularly prone to *calcification* of fatty or lipoid material.

Myxomatous Cysts

Myxomatous cysts are found sporadically on the labia minora or on the folds between the labia majora and minora. They present a vesicular or bullous aspect and contain a translucent whitish to yellowish mucous or gelatinous mass, or incidentally a bloody serous fluid. Histologically they show a fibrous wall, with one or more layers of cylindrical, ciliated or non

ciliated cells These cysts are either malformations or are derived from aberrant embryonic cell elements They must be distinguished from reten tion cysts such as cystic degenerated Bartholin glands or cysts developing after birth trauma of the posterior commissure by obliteration of the Bartholin duct (see Chapter 18)

Supernumerary Mammary Gland Tissue

Exceptionally supernumerary mammary gland tissue has been found embedded in the vulvar tissues These congenital inclusions form lumps located directly under the skin. They may proliferate J H. Fisher described such a case in a woman of forty seven years The tumor was detected during a hysterectomy for uterine fibroids Histologically it presented the features of a benign pericanalicular fibro-adenoma

Pigmented Nevi

As elsewhere on the body pigmented nevi (moles) are also found in the genital or surrounding regions in both sexes. Flat or slightly elevated brown nevi and nevi pilosi apparently predominate. In females pigmented nevi may deepen in color during pregnancy Less frequent but of greater importance are the deep brown, black, or bluish black *melanotic nevi* notorious for their potential malignancy

The site and distribution of many pigmented nevi seem to follow a phylogenetically fixed linear system (Nevus linien) which plays such a significant role also in the distribution of pigmentation in animals The inguino-genital and lumbosacral regions are sites of predilection for these systematized nevi. The *giant swimming* trunk nevus covers *the entire* circumference of the lower sections of the trunk, including the genital region, thus forming an enormous nevus mass of dark brown color with all the features of an elevated nevus pigmentosus et pilosus Its surface is uneven, usually showing warty prominences. The phylogenetical relations of these anomalies and their similarity to the cutaneous configuration pattern in animals have been explained in a classical monograph by E Meirowsky *and L. Leven (1921)*

Differential diagnosis: Usually the patient s history indicates the con genital nature of the lesions However a distinction of the various types of benign genital neoplasms depends largely upon microscopical studies. It may be impossible to determine their origin before serial examination after total excision. Even a careful histological investigation may not permit a conclusive definition of certain tumor forms, such as sweat gland tumors or genital cysts, and may not suffice for an early recognition of transitional stages from benign to malignant structures.

Fibrolipomas and lipomas of the labia majora must be differentiated

from congenital hyperplasia of the labia, which occurs as an individual or familial anomaly Angiomas and massive lymphangiomas can be flattened, receding markedly in volume under continuous pressure and returning to their previous size following release of pressure.

Treatment: Radical excision of melanotic nevi of the genitals should be performed early as a preventive measure. The management of hemangiomas and lymphangiomas of the genitals is in line with generally accepted procedures, such as refrigeration by solid carbon dioxide (for superficial lesions) sclerosing solutions such as injections of 30 per cent invert sugar solution, but combined with 10 per cent sodium chloride) and primarily radium therapy Many of the discussed neoplasms are highly radiosensitive. However as stated by Costello, except for superficial forms, every case of hemangioma is a law unto itself This applies likewise to the genital location of angiomas

B Malignant Neoplasms of the External Genital Region

Introduction
Erythroplasia, Bowen and Paget Diseases
Basal Cell Epithelioma
Carcinoma Penis
Malignant Melanoma
Sarcomatous Tumors of the Penis
Scrotal Cancer
Carcinoma Vulva
Sarcomatous Tumors of the Vulva

Introduction

The purpose of this chapter is to describe the various manifestations of *cancer* of the genital region and, at the same time, to call attention to some peculiarities arising from this particular location of the malignant growth. The diagnostic significance and the differentiation from other nonvenereal conditions of the penis, scrotum and vulva have been the major determinants in this description.

Omitting any discussion of the great general problems of cancer pathology and classification, we are here chiefly concerned with the *primary* malignant neoplasms of the external genitals especially the various forms of epithelioma involving the genital integument. Comparatively malignant growth invading the genital skin from adjacent or more deeply located cancer by extension via the lymphatics (cancer of the prostate, rectum or testicles) and metastatic carcinoma reaching the genitals from distant tumors elsewhere in the body via the blood stream, appeared here of secondary importance

The differential diagnosis between malignant processes and other genital lesions have been discussed in several previous chapters. The present section will be devoted to elaborate upon and supplement earlier statements

Detection of the very first symptoms of *primary* cancer of the external

genitals is difficult, if not impossible since, especially in this region of the body an initially inconspicuous, painless nodule or erosion easily escapes the patient's attention. On the other hand, cancerophobia may often develop in the presence of chronic genital ulcers or proliferations that fail to respond to treatment. Many persons of the laity know very well that chronic lesions of the glans prepuce or vulva may develop into carcinoma.

The physician when asked for advice may be confronted with intricate diagnostic problems Well aware of the potential malignancy of certain chronic genital affections it is imperative that he come to an early decision as to whether or not an actual state of malignancy exists.

A more or less marked malignant potentiality has been ascribed to numerous chronic affections of the external genitals but the incidence of actual malignant transformation varies widely and largely in proportion to the incidence of the respective lesions themselves In the World literature such cutaneous affections are frequently dealt with collectively under the heading of "*precancerous conditions* usually a misnomer in consideration of the fact that malignant transformation although possible, will not necessarily develop in a single instance

The designation precancerous is questionable likewise because the borderline between cancerous and non-cancerous changes frequently remains indefinite even following the careful study of serial sections of biopsy material.

Striking discrepancies occur between the clinical and histological features Thus an exuberant, condylomatous growth may simulate carcinoma of the penis, while careful microscopical examination reveals only chronic inflammatory changes, acanthosis or dyskeratosis On the other hand, proliferations clinically typical of pointed condyloma acuminatum occasionally show microscopic evidence of malignancy

Considering the difficulties in determining the actual onset of malignant growth, many dermatologists and surgeons classify those genital affections which, almost as a rule undergo cancerous transformation, as malignant. Thus many surgeons and dermatologists consider Queyrat's erythroplasia, Bowen's and Paget's diseases of the penis and vulva, not as "precancerous, but a priori as cancerous affections. This opinion is reflected also in the foreign nomenclature. French authors classified these conditions as variants of a special type of epithelial cancer ("cancer des dyskératoses or "malignant dyskératoses Ash) From this point of view Queyrat's Bowen's and Paget's diseases will be included in this chapter

Leucoplakia vulvae and leucokeratosis penis well known as possible starting points of cancerous growth, have been discussed in Chapter 14. In other conditions such as balanitis xerotica obliterans or kraurosis glandis

et praeputii, malignant transformation is more exceptional. However conclusive statistics are lacking for rare and less known genital conditions.

The role of chronic, relapsing balanoposthitis and phimosis in the pathogenesis of penile cancer will be explained in this chapter. We have previously referred to the diagnostic importance of occupational cancer of the scrotum due to chronic exposure to coal dust or to certain chemicals.

As elsewhere on the body so also in this region cancer may develop from chronic inflammatory lesions due to tuberculosis (lupus) bilharziasis, filariasis leprosy or lupus vulgaris Roentgen and radium burns of the anogenital skin may give rise to cancerous growth Congenital anomalies, such as nevi, and in particular melanotic nevi, or benign tumors (angiomas, fibromas) of the external genitals may undergo malignant transformation.

Erythroplasia

Queyrat's erythroplasia had been described already in the ancient literature as epitheliome bénin syphiloide de la verge (Fournier and



FIGURE 110 Erythroplasia of the glans. (Dermat Clinic Univ of Naples, Prof Dr M Monacelli.)

Darier 1893) Queyrat, in his classical study (1911) first used the term érythroplasie (erythroplasia) Sulzberger and Satenstein (1933) described the first case of erythroplasia in the American literature

In the majority of cases, this condition involves the glans and coronal

sulcus less frequently the prepuce and only exceptionally the shaft of the penis Erythroplasia develops as a circumscribed, flat pink or red velvety patch. The affected area of the skin is pliable Superficial erosions may occur The patch increases slowly up to a certain size and then remains unchanged for an indeterminate period unless malignant transformation takes place The marked tendency of erythroplasia to malignant degenera

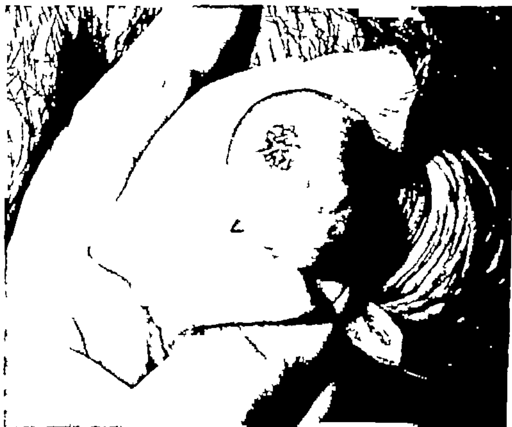


Figure 111 Erythroplasia penis. (Department of Dermatology and Syphilology of the New York University Post-Graduate Medical School, Dr Marion B Sulzberger Chairman, and the Skin and Cancer Unit of the New York University Hospital.)

tion has led to the assumption by foreign and especially French authors, that cancer will develop in every case of erythroplasia, provided the patient s lifespan be long enough

Histology: Irregular downgrowth of the rete pegs with changes of the epithelial structure irregular accumulation of cell elements resembling partly malphigian, partly basal cells inflammatory infiltration containing many plasma cells (Kolb McDaniel and Mason) In later stages cells with large clumping nuclei, suggestive of Bowen s disease, may be found. For

this reason Civatte believed Queyrat's erythroplasia to be identical with Bowen's disease.

Etiology: The etiology is unknown.

Differential diagnosis: The differentiation of erythroplasia from other genital diseases will involve exclusion of Bowen's and Paget's diseases, lupus vulgaris psoriasis, eczematous changes and syphiloma. In the

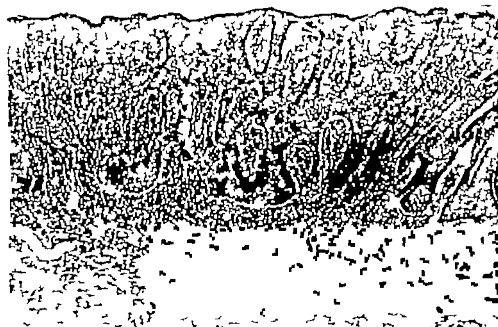


FIGURE 112. Microscopic picture of erythroplasia penis. (Department of Dermatology and Syphilology of the New York University Post Graduate Medical School, Dr Marion B Sulzberger Chairman, and the Skin and Cancer Unit of the New York University Hospital.)

absence of other manifestations of these diseases a definite diagnosis requires microscopic examination to exclude a possible malignant lesion Erythroplasia is microscopically distinguished from Bowen's disease by the presence of the rolled up margins of Bowen's patches In Paget's disease ulcers which are very rare in erythroplasia are common. As previously explained, histological differentiation of Queyrat's erythroplasia from Bowen's disease is sometimes impossible

Therapy: Surgeons believe that erythroplasia should be treated from the beginning as a malignant disease by total excision or local destruction by radium, Roentgen rays or electrosurgery Any form of irritating local treatment is definitely contraindicated.

Bowen's Disease

Bowen's disease (*dyskeratose lenticulaire et en disque* Darier 1914) consists of solitary or multiple, more or less elevated, irregular red hyperkeratotic patches. The lesions may become crusted or scaly. They may remain stable for long periods. The transition of Bowen's lesions into



FIGURE 113 Bowen's disease (Department of Dermatology and Syphilology of the New York Post Graduate Medical School, Dr Marion B Sulzberger Chairman, and the Skin and Cancer Unit of the New York University Hospital.)

squamous cell cancer has been estimated to occur in about 25 per cent of all cases reported, granted a prolonged observation period. For this reason, many surgeons and pathologists have preferred to classify Bowen's disease as an intra-epithelial type of squamous cell cancer or plainly as *intra-epithelial cancer*

Bowen's disease of the *penis* was first described by Jessner (two cases 1921) and on the *vulva* by Hudelo *et al.* (1922) Kleeberg described a case

in a man of seventy five years, presenting a lesion of about 3 × 4 cm. in circumference, involving the glans up to the coronal sulcus. The central part of this lesion was depressed, the margins infiltrated and elevated. Scommazoni observed three patients with Bowen's disease of the penis, the oldest of them showing a dark red, infiltrated patch with scaling of the elevated margins. This lesion involved the internal lamina of the prepuce and was associated with a similar lesion of the glans.

Histology: Intracellular edema and inflammatory infiltration of the corium marked dyskeratosis with findings of large, irregular cells with

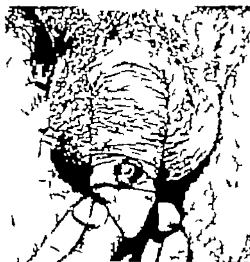


FIGURE 114. Bowen's disease of the prepuce of an 81 year-old man. (Scommazoni, T *Gior Ital. Dermat e Syph., 81* 1927 Fig. 20)

giant "clumping" nuclei. The latter cells are characteristic of Bowen's disease.

Malignant transformation is apparently only a matter of time, although years may pass before changes become evident. Bowen's disease has been generally recognized as the initial or a preliminary stage of squamous cell carcinoma.

Paget's Disease

Paget's disease of the genitals, one of the extra-mammary locations of Paget's disease of the nipple, has been described by Paget himself In his case the *penile* lesion resembled the breast affection in every respect. A long persisting balanitis with soreness of the lower lip of the meatus had preceded the onset of symptoms. Susman reviewed thirty four cases of Paget's disease, of which fourteen involved the genitals and of the latter seven involved the penis. One of Susman's patients a man of sixty years, complained of an itching eruption around the meatus of about one year's

duration. Examination revealed a dark red, well circumscribed and slightly indurated lesion with a finely granulated surface

Histological examination reveals the presence of Paget's cells i.e. *round cells of larger than normal size with a clear homogenous protoplasm* and deeply stained nuclei. Vacuoles are characteristic of these cell elements Their connections with the normal prickle cells are loosened, thus changing the epidermal structure.

Like Paget's disease of the nipple, so also extra mammary Paget's disease may develop from a circumscribed weeping or encrusted lesion resembling an eczematous process. A slight, parchment like infiltration of the base of such eczematoid patch may point to its different pathogenesis.

Differential diagnosis: It is not always possible to distinguish microscopically between Bowen's and Paget's diseases of the genitals in all stages of their evolution. Both conditions run the same slow course Even *histological differentiation may prove difficult. Dyskeratosis in its various* stages, is characteristic of both affections The extent and distribution of edema and inflammatory infiltration are not decisive A definite diagnosis is justifiable only when either the typical "clumping cells or Paget cells dominate the histological picture.

The differentiation of Bowen's disease from Queyrat's erythroplasia of the penis has been discussed on page 217 Occasionally Bowen's disease must be distinguished from certain forms of tertiary syphiloma. Here biopsy will solve the diagnostic problem. A biopsy should always be performed

Therapy: The early destruction or wide excision of Bowen's and Paget's lesions or of basal cell epithelioma without lymphadenectomy has been generally recommended. Only if the regional lymph glands appear obviously involved, is radical surgery including removal of all regional lymph glands indicated. As a matter of fact Bowen lesions may form on *other places of the genital region after complete removal of a single lesion*

Basal Cell Epithelioma

The basal cell epithelioma commonly seen on the face nose or forehead is infrequent in the genital region and its surroundings, but exceptionally occurs there as elsewhere on the body

The grayish, warty initial lesion grows very slowly with a tendency to ulceration of its central portion. A firmly adherent crust soon covers the lesion. Its border appears rolled up and encircles the ulcer as a firm, pearly margin. *Microscopically the margin is found to enclose con*glomerations of cornified epitheliomatous cells. During the chronic course some part of the lesion may undergo cicatrization. The destructive process prevails however and may involve the underlying tissues. As a rule, the

common type of basal cell epithelioma does not metastasize. However its designation as "benign" basal cell epithelioma sometimes encountered in the literature, should be used with the greatest reservation regarding the occasional occurrence of transitional forms.

Histology: The basal cell epithelioma shows a varying arrangement of basal cells of an embryonal character the latter are derived from the basal cells of the epidermis. There are also spindle-shaped cells with small oval nuclei, rich in chromatin, with little tendency to cornification. A possible origin from the dorsal appendages can not be excluded. This conclusion, however can hardly be drawn from biopsy specimens taken from a fully



FIGURE 115 Basal cell epithelioma, perianal. (Dermat. Clinic, Frankfurt, Prof Dr O Gans.)

developed basal cell epithelioma. The presence of the "epithelial pearls mentioned above, is of significance.

Differential diagnosis: It is necessary to differentiate basal cell epitheliomata of the anogenital region from Bowen's and Paget's disease. Biopsy is imperative. Paget's disease is extremely rare in the male. Each of the three lesions mentioned presents characteristic cell forms the Paget cells, Bowen's clumping cells and the solid, epitheliomatous growth of basal cells derived from the basal cell elements of the epidermis. Paget's cells and clumping cells are never found in basal cell epithelioma the multiform shape of cells and nuclei so significant in Bowen's disease is lacking

Transitional forms: Occasionally an externally typical, basal cell epithelioma may change its course growing rapidly to form a large and deep fungating ulcer with purulent secretion. Enlargement of the inguinal glands and the formation of metastases may follow As H Montgomery has emphasized, microscopical examination of such epitheliomata may reveal them to be in fact "basal squamous or squamous carcinomas. About 20 per cent of all neoplasms diagnosed clinically as basal cell epitheliomas, are transitional forms between basal and prickle cell epitheliomata (H.

Montgomery) Such neoplasms occur sporadically on the penis the vulva and in the perianal region they develop chiefly near the natural orifices of the body

Squamous Cell Carcinoma of the Penis

Incidence and age: Carcinoma of the penis constitutes from 1 to 3 per cent of all carcinomas in men (Harlin 1925) In a series of one hundred twenty cases of penile cancer treated at the Memorial Hospital of New York City Dean (1935) accordingly calculated that they represented 1.25 per cent of all malignant tumors in men and 2 per cent of all tumors of the genito-urinary tract in both sexes These figures correspond approximately to the statistical findings of many other authors

Squamous cell carcinoma of the penis develops chiefly in the fifth or sixth decades of life, occasionally in younger individuals and exceptionally in persons under twenty five years of age (the average being fifty years in the above mentioned series by Dean)

Etiological factors: Clinical experience indicates a close direct relation of carcinoma of the penis to chronic irritation and inflammation of the glans and prepuce. Phimosis and relapsing balanoposthitis are considered to be predisposing factors. As a matter of fact chronic phimosis is the usual antecedent of penile cancer

The question arises *will early circumcision prevent cancer of the penis?* In orthodox Jews, who are subjected to ritual circumcision eight days after birth, carcinoma of the penis occurs rarely if ever On the other hand, in Moslem populations where this operation is performed at the ages of two to fourteen years penile cancer has been observed in later life after intervals of eight to forty-one years (E. L. Kennaway) Furthermore, cancer of the penis is very common among some people in Asia, who do not practice circumcision In addition Kennaway reported sixteen cases of penile carcinoma following surgical circumcisions in patients from fourteen to forty five years of age.

Kennaway brought up the question as to whether penile cancer can be provoked due to chronic irritation by some purely external agent, just as scrotal cancer is produced by the effects of soot, petroleum, tar products, etc. The obvious influence of phimosis in the pathogenesis of penile cancer suggests the possibility of some carcinogenous agent formed in the substance between the glans and prepuce. Plaut and Kohn Speyer succeeded in producing cancer in mice experimentally by implantation of horse smegma into dorsal tunnels of the epidermis, whereas control mice of the same strain did not develop cancer

In relation to the argument that a circumcised individual is exposed "not less, but more to external irritations from which an unretracted pre-

puce should protect the penis Kennaway refers to Dean s statement that following circumcision, a gradual thickening of the epidermis takes place. This thickening may explain an increased resistance to cancer formation in persons subjected to early circumcision.

Clinical symptoms: The sites of origin of carcinoma of the penis are the inner sheath of the prepuce, the coronal sulcus the glans near the urethral meatus and occasionally the shaft of the penis. The initial lesion is a minute, scaling patch a warty or nodular lesion or an inconspicuous ulcer It may escape the patient s attention for a long time, especially when hidden beneath an irretractable prepuce. Slowly increasing in size or multiplying and coalescing into a larger patch, the primary lesion develops into one of the various clinical types of carcinoma of the penis.



FIG. 116 Epithelioma of penis, ulcerative stage (Moulage Dermat. Clinic, Breslau, Prof Dr J Jadassohn.)

Following Herbut s recent description, carcinoma of the penis may present:

(1) A *fungating* form with papillomatous proliferations of grayish white color large parts of the glans and prepuce may be involved. For a long time, this mass may remain movable over the underlying tissue, but at a later stage it becomes firmly attached The irregularly lobulated tumor may show superficial ulceration. A malodorous discharge covers the tumor mass.

(2) An *infiltrating* type, differing from the fungating form by its extreme firmness and infiltrating expansion A solid indurated mass develops attached to the underlying tissue The process may include the spongy body of the glans, and, in more advanced stages the cavernous bodies of the penis. The surface of the tumor appears finely or coarsely granulated. A purulent or sanguinolent discharge covers the surface

(3) An *ulcerating* type, commencing as a small ulcer which increases in size to form a large sharply demarcated, crater like ulceration surrounded by a firm, elevated wall of neoplastic tissue. The grayish white, more or less friable cancer tissue covers the base, while the peripheral part of the ulcer may be covered by a smooth raised epidermis.

The great majority of squamous carcinomas of the penis show a Broder malignancy of Grade two Buck's fascia presents a natural barrier to the spread of the tumor once this barrier has been broken through, propagation appears to progress more rapidly (Dean, Herbut, *et al*)

The penis is abundantly supplied by lymphatics. Finally in most cases the lymph glands become enlarged apparently earlier in the infiltrating and ulcerating than in the fungating forms. Hematogenous metastases may follow

Subjective symptoms: These vary according to the location, stage and type of the malignant growth In the presence of phimosis, there may be burning and itching associated with painful micturition. A foul, purulent or bloody discharge causes the patient to seek medical advice On admission the patient may already have observed a lump palpable beneath the irretractable prepuce in other cases, large ulcers and not infrequently urinary fistulas are already present at the first consultation.

Histology: The parenchyma of squamous cancer is formed chiefly of the prickle type of cell. These cells differ in size and shape from normal prickle cells Large cell forms and mitoses are found especially among the cancer cells lying free in the tissue A marked polymorphism of the proliferating cells is characteristic of squamous cancer

Differential diagnosis: Diagnostic problems may be presented in the various stages of carcinoma of the penis, or by the scaly or nodular initial lesion as well as the papillary and ulcerating forms of advanced cancer Differential diagnosis includes syphilitic chancre and late syphilomas (gummas) tuberculosis granuloma inguinale and chronic genital ulcers of many other types.

Of foremost importance is the differentiation between papillary cancer and condyloma acuminatum this problem has been discussed previously (Chapter 4)

The distinction between *syphilomas* and cancerous growth of the penis is often difficult Sometimes a patient may be afflicted simultaneously by syphilis and penile cancer Unfortunately as remarked by Dean serologic tests "are so much more conveniently performed than tissue biopsies He warns against time-consuming, antisyphilitic therapeutic tests, while the tumor propagates unchecked Both diseases produce circumscribed, indurated lesions, with destruction of the underlying tissues. Biopsy is indispensable

Histologically it is frequently hardly possible to draw a sharp line between syphilitic and cancerous proliferation. Syphilis as well as tuberculosis, may cause atypical, epithelial proliferations resembling a beginning blastoma. Furthermore, the demarcation of cancerous growth from the stroma gradually vanishes when the connective tissue reaction results in a dense lymphocytic and plasma cell accumulation, covering the invasion of the cancer cells

Recent authors have directed attention to the association of squamous carcinoma with the anogenital manifestations of *lymphogranuloma venereum* (Delbert and Greenblatt, Guzman, *et al.*) This combination happens not only as a casual coincidence, but also as a manifestation of malignancy developing in the anogenital lesions of lymphogranuloma venereum. Guzman reported on vulvar Binkley and Derrick on anal manifestations of both diseases in the same individuals An early recognition of malignancy may be difficult in the ulcerating and fungating types of vulvar and anal lymphogranuloma lesions. In other cases squamous carcinoma of the anogenital region may be mistaken for lymphogranuloma venereum in the presence of a positive Frei test. Beerman issued a warning against the danger of relying too much upon a positive Frei test in a patient without a suggestive history or other clinical evidence of lymphogranuloma venereum.

The differentiation between cancerous growth and the nodular or ulcerovegetative forms of *granuloma inguinale* depends essentially on biopsy Smears stained by Wright's method may reveal the presence of Donovan bodies within mononuclear cells. Histologically a dense accumulation of plasma cells beneath the epidermal layers is characteristic of granuloma inguinale. An intense lymphocytic infiltration of the corium may present the picture of an infectious granulation tumor There is no atypical cell proliferation as in carcinoma of the penis.

Treatment of carcinoma of the penis: Basal cell epithelioma, occasionally occurring in the anogenital region, should be removed by total excision. Irradiation is reserved for basal cell epitheliomata less amenable to surgery (glans penis) As a rule superficial basal cell epithelioma responds promptly to radium therapy Cases which show incomplete or no reaction to radium application will usually be found to be transitional forms of basal squamous structure

Amputation of the penis is the method of choice for carcinoma of the penis Partial amputation will suffice in the majority of carcinomas limited to the distal end of the penis. Conservative amputation has been strongly recommended by Dean It may suffice to preserve at least 1.5 cm. *proximal to all visible or palpable changes, thus leaving an adequate stump* to provide sufficient urethral mucosa to permit unhampered micturition.

(3) An *ulcerating* type commencing as a small ulcer which increases in size to form a large sharply demarcated, crater like ulceration surrounded by a firm, elevated wall of neoplastic tissue The grayish white more or less friable cancer tissue covers the base while the peripheral part of the ulcer may be covered by a smooth, raised epidermis

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The penis is abundantly supplied by lymphatics. Finally in most cases the lymph glands become enlarged, apparently earlier in the infiltrating and ulcerating than in the fungating forms Hematogenous metastases may follow

Subjective symptoms: These vary according to the location, stage *and type of the malignant growth. In the presence of phimosis there may* be burning and itching associated with painful micturition. A foul, purulent or bloody discharge causes the patient to seek medical advice On admission the patient may already have observed a lump palpable beneath the irretractable prepuce in other cases large ulcers and not infrequently urinary fistulas are already present at the first consultation

Histology: The parenchyma of squamous cancer is formed chiefly of *the prickle type of cell. These cells differ in size and shape from normal* prickle cells Large cell forms and mitoses are found especially among the cancer cells lying free in the tissue A marked polymorphism of the proliferating cells is characteristic of squamous cancer

Differential diagnosis: Diagnostic problems may be presented in the various stages of carcinoma of the penis or by the scaly or nodular initial lesion as well as the papillary and ulcerating forms of advanced cancer *Differential diagnosis includes syphilitic chancre and late syphilomas* (gummas) tuberculosis, granuloma inguinale and chronic genital ulcers of many other types.

Of foremost importance is the differentiation between papillary cancer and condyloma acuminatum this problem has been discussed previously (Chapter 4)

The distinction between *syphilomas* and cancerous growth of the *penis is often difficult. Sometimes a patient may be afflicted simultaneously* by syphilis and penile cancer Unfortunately as remarked by Dean serologic tests are so much more conveniently performed than tissue biopsies He warns against time-consuming, antisyphilitic therapeutic tests, while the tumor propagates unchecked. Both diseases produce circumscribed, indurated lesions with destruction of the underlying tissues Biopsy is indispensable.

If not arising from a clinically manifest nevus, the malignant melanoma begins as a solitary blue-black or brownish black, flat or elevated patch or nodule. It grows rapidly to a solid black tumor mass The malignant transformation of a previously benign pigmented nevus manifests itself by a rapid increase in size, increased pigment formation an inflammatory appearance, a verrucous surface and subsequently by a rapid propagation of the tumor Ulceration may occur

Malignant melanoma of the penis or vulva tends to produce early metastases involving the lymph glands the skin and internal organs. Most of the untreated cases run a fatal course within a few years following the discovery of malignancy In other instances a fulminating onset of metastases precipitates the fatal issue. Melano-carcinomas of the mucous membranes when located in the genital or anorectal region are almost uniformly fatal.

Histology: In biopsy specimens taken at an early stage of malignant melanoma, it may be possible to follow the process of the malignant transformation of a pigmented nevus The starting point will be found in the deepest epidermal layers. Characteristic detachments of single or grouped epithelial cells are seen at the border between epidermis and corium (Unna, Delbanco Kyrle Gans) The loosened cells change to atypical cells of various shape, filled with melanin masses and crystalline lipoids. An intense infiltration with lymphocytes, plasma cells, and chromatophores soon dominates the picture. Pigment-carrying cells appear free in the corium. Occasionally an interstitial edema may cause a complete loosening of the epidermis from the underlying stroma.

The question in a given case, as to whether malignant melanoma of the penis or vulva may be of epidermal or mesodermal origin is of little practical importance This problem is still a matter of discussion. The determining factor is the type of the mother cell of the neoplasm. Malignant melanomas of epitheliomatous character seem to prevail Melanotic tumors suggesting a *sarcomatous* type are usually derived from a blue nevus (Jadassohn) As Beerman explains, the term malignant melanoma suggested by Becker is non-committal it relieves the investigator of definite classification in an individual case.

Differential diagnosis must include the benign pigmented nevus, verruca senilis and angiomatous tumors. Biopsy is decisive

Treatment: Every pigmented nevus of the anogenital region, exposed to irritation by friction sweat or discharge should be promptly removed. At the time of the slightest manifestation of an increase in size or pigmentation excision becomes imperative After the verification of malignancy by biopsy surgical treatment is indispensable. Surgical removal should follow immediately after verification of malignancy Local treat

ment with electrocoagulation or Roentgen irradiation has been disapproved by many surgeons. Excision must be radical and should include dissection of the regional lymph glands in every case suggesting metastases. In spite of this procedure, prognosis is poor The reader is referred to Savran and associates in *Am J Surg* 75 743 1948, and to Allen and Spitz, *Cancer* 6 1–45 1953

A patient of fifty-nine years under our observation showed a bluish melanotic tumor on the mons pubis near the root of the penis, which had its origin in a pigmented nevus Radical excision and bilateral dissection of the groin was followed by multiple cutaneous metastases around and at a distance from the unchanged operation scar Death, six weeks after admission.

The risk of a possible explosive eruption of metastatic nodules in the surroundings of the operative scar should be taken into consideration in an individual case This refers especially to the slowly progressing malignant melanomas of advanced age or to surgically inaccessible melanomas of certain cutaneous regions (nose naso-labial folds, vulva) Reservation appears indicated in those instances.

Sarcomatous Tumors of the Penis

Incidence and age: As compared with squamous carcinoma, sarcomatous tumors of the penis are rare. Case reports of primary sarcoma of the penis are scarce Judging from the reports available, the age incidence varies from thirty five to sixty years. These tumors may be hemangio-endotheliomas rarely spindle-cell sarcomas, or fibro-sarcomas exceptionally myosarcomas, or mixed forms.

Sarcomatous neoplasms of the penis, although similar in their external appearance, present certain peculiarities due to their location. These tumors are derived from the mesodermal tissues of the organ, frequently involving or originating from the corpora cavernosa penis and urethrae.

Deviations on erection and priapism may be the first symptoms causing the patient to seek medical advice. A great variety of indurative processes of the penis may result in impaired erection and sexual impotence. This will be discussed in Chapter 20 (section on induratio penis plastica)

Clinical symptoms: An inconspicuous, warty papillary or nodular lesion may have been present on the glans for many years without causing any discomfort Enlargement of the anterior part of the penis and some discharge will attract the first attention of the patient This discharge may become bloody in addition, pains and difficulty on urination may demand medical advice Hemangio-endotheliomas usually manifest themselves by a nodular induration beneath the freely movable skin. Gradually increasing in size, such induration changes to a rounded smooth mass sometimes

up to the size of a pigeon's egg. They may differ in consistency Instead of a circumscribed tumor multiple small indurations may be palpable. The indurations are painless and are not tender on manipulation.

Usually sarcoma of the penis grows very slowly Growth may be stimulated by improper removal of the initial lesion This was the case of a patient of Joelson. Becoming aware of a papillary proliferation on the glans the patient cut off the lesion with a scissors. The remaining base was soon transformed into a large ulcerating and fungating tumor (fibrosarcoma)

The most malignant type of sarcoma penis is the *endothelioma* of the penis, the least common type among all penile sarcomas. Coppridge Putman and Miale studied twelve cases average duration of life after onset of symptoms eight to thirty four months

A characteristic case described by Kreibig, illustrates the appearance and course of an *hemangio-endothelioma* of the penis Three years before admission a man of thirty five years had been circumcised for removal of a firm nodule hidden under the prepuce. No biopsy was performed at that time. A sharply demarcated flat induration of a shilling's size was felt under the movable skin. Biopsy revealed a purely fibromatous structure. Clinically and histologically induratio penis plastica appeared evident. There was no response to radium therapy Subsequently a solid tumor mass developed, involving the distal third of the penis, with stenosis of the meatus and formation of a urinary fistula. Amputatio penis was performed. A cross section of the organ showed a streaky grayish neoplastic tissue, wrapping the urethra like a cloak, and extending into the corpora cavernosa. Only a few cavernous spaces were demonstrable on microscopic examination

Hemangio-endothelioma metastasizes early On the other hand, fibrosarcoma of the penis may remain confined to this organ for an undetermined period, metastases being a rare complication Notwithstanding many similarities of their clinical features, the manifold forms of penile sarcoma vary largely in histological aspect. Their microscopical structures do not differ from cutaneous sarcoma elsewhere in the skin. Detailed information is presented in surgical and urological monographs.

Differential diagnosis: Sarcomatous tumors of the penis must be distinguished from various indurative processes of the penile tissues caused by infectious diseases such as syphilis and lymphogranuloma venereum or by thrombosis.

The differential diagnosis of hemangio-endothelioma includes vascular sarcoma, hemangioma and exceptionally Kaposi's disease, which was observed as a penile affection by Barringer and Dean in 1935 The distinction of endothelioma from induratio penis plastica is based upon the different courses of the two conditions. The discrete indurations of the latter affection

develop slowly and usually persist unchanged for years. They present nodular or flat, shield like formations derived from the tunica albuginea of the cavernous bodies

Sarcomatous transformation of pre-existing fibromas or neurofibromas of the genital region occurs occasionally in connection with generalized neurofibromatosis (von Recklinghausen) In such a case, Haines and Garvey (1950) found a neurosarcoma of the penis associated with multiple fibromas and café au lait spots Beneath the prepuce a firm tumor was seen consisting of several nodular masses Histologic examination following amputation revealed a neurofibrosarcoma

Treatment of sarcoma of the penis is surgical. Amputation should be performed according to the principles discussed in connection with car cinoma of the penis

Cancer of the Scrotum

Except as an occupational disease due to prolonged irritation by soot, *tar pitch paraffin and other carcinogenic agents scrotal cancer is very* rare. The age incidence as cited in available reports, ranges from thirty



FIGURE 117 Paraffin cancer of scrotum. (Dermat Clinic, Leipzig, Prof Dr J H Rille)

two to seventy six years Beginning as a circumscribed induration, car cinoma of the scrotum usually spreads by way of the lymphatics. Hema togenous metastases may occur in the terminal stages.

Due to the achievements of Industrial Medicine in controlling the health of industrial workers occupational cancer of the scrotum has become a very rare condition in the United States Besides the above named irritants, the continuous contact with petroleum and its products remains the most common cause of scrotal cancer in the New York area (Rolnick)

Chimney-sweep's cancer and the mule-spinner's cancer of earlier times are today extremely rare in the United States.

The preliminary symptoms of *occupational cancer of the scrotum* include itching, *scaly eczematous lesions, erosions and rhagades and warty or* papillary changes. Ulceration is the most alarming signal of a possible malignant process. The most dependent part of the scrotum appears to be most frequently involved. Similar cutaneous symptoms may however extend to the penis. In the majority of cases, a prolonged exposure precedes the onset of serious changes. The ulcers forming in advanced stages are painless, until a purulent or sanguinolent secretion causes burning and pains.

Histology: The epitheliomatous tumors of scrotal occupational cancer usually present a stratified type of squamous cancer with distinct pearl formations associated with various degrees of lymphocytic and plasma cell infiltration (Herbut)

Diagnosis may be self-evident from the history of the patient. Otherwise any stage of a scrotal carcinoma will demand differentiation from eczematous hyperkeratotic and ulcerative lesions of the scrotal skin. Biopsy is imperative.

Treatment: The prophylaxis of occupational cancer is discussed in the literature on industrial medicine. Wide excision is strongly indicated for *primary scrotal cancerous tumors, including a dissection of the regional* glands if metastasis is suspected or evident. Roentgen irradiation as a postoperative treatment for occupational cancer of the scrotum has been advocated by many radiologists and surgeons.

Cancer of the Vulva (Carcinomae Vulvae)

Incidence: As compared with carcinoma of the uterus primary carcinoma of the vulva is very rare a ratio of 1 35 to 40 having been estimated by Virchow and Burghele of 1 29 by O Frankl, and of 1 40 by Brady etc. Statistically vulvar carcinoma constitutes not more than 1 to 3 per cent of all carcinomas of the female genitals.

Age: Carcinoma of the vulva is a disease of advanced age, occurring predominantly after the menopause, i.e., during the sixth and seventh decades of life or later less frequently during the fifth decade and rarely in younger women Sporadically it has been observed in virgins of fifteen to eighteen years of age. It is particularly carcinoma of the clitoris, that may afflict women under forty years.

Clinical manifestations: The malignant process begins in the skin or in the mucosa of the vulva. It may originate in a pre-existing pigmented nevus or leukoplakia (see Chapter 14) Usually the initial lesion is found on the inner aspect of the labia majora, less frequently on the labia minora.

the clitoris or around the urethral meatus (borderline between the squamous epithelium of the cutis and the cylindrical epithelium of the mucosa)

The initial lesion seldom comes to the physician's attention The first symptom leading the patient to seek medical advice in carcinoma of the vulva may be only a more or less intense pruritus or a sensation of soreness In addition the patient may have noticed a nodule wart or a small open wound.

On admission, a solid, smooth dull nodule about the size of a walnut will be found or in other cases a more diffuse nodular induration palpable beneath the movable skin or mucosa. A marked tendency to ulceration soon changes the aspect of the initial lesion. The tumor breaks down into a crater like discolored ulcer with an uneven tuberous base exuding a purulent or bloody discharge Or a papillary growth may develop producing a large cauliflower like mass, not infrequently simulating condyloma acuminatum

In the majority of cases and especially in younger women *carcinoma of the vulva*



FIGURE 118. Squamous cell epithelioma, perianal region, same patient as Fig. 119



FIGURE 119 The same patient as Fig. 118, microscopic picture.

runs a rapid course Two clinical patterns may develop i.e., a fungating form, or an infiltrating ulceration. Carcinoma of the clitoris and vulvo-urethral carcinoma are notorious for their rapid spread owing to the abundance of deep blood and lymph vessels in the involved areas Furthermore, this location of malignancy implicates early involvement of the inguinal and crural glands. On the contrary primary carcinoma of *Bartholin's glands* and *malignant hidroadenoma* of the vulva run a slower course owing to the retarding effect of the periglandular capsules (see Chapter 18) The initial nodule of a primary tumor of Bartholin's gland may escape the patient's attention for a long time.



FIGURE 120 Squamous cell epithelioma of the vulva clinically resembling condyloma acuminatum. (Dermat. Clinic, Frankfort, Prof Dr O Gans.)

In carcinoma of the clitoris, the average survival following onset of symptoms rarely exceeds fifteen to eighteen months.

Vulvar carcinomas metastasize early by dissemination through the lymphatics or through the blood stream The inguinocrural glands may appear unchanged at a time when a histologic study of autopsy specimens shows definite carcinoma.

The *histopathology* of carcinoma vulvae is discussed in the gynecological literature The majority of cases represent carcinomas of the squamous cell type with an occasional adenocarcinoma.

Sarcoma of the Vulva

Primary sarcomatous tumors of the vulva are rarities. They most frequently involve the labia majora. The primary lesion consists of a solid

nodule beneath the movable skin. Growing rapidly this nodule is soon transformed into a large smooth, roundish and tuberous yellowish to red tumor *Hemorrhages and necroses may* change the appearance of such tumors The primary nodule may persist over a long period, before the sudden onset of rapid growth.

Sarcomatous growth originates quite frequently in pre-existing fibroma or fibrolipoma of the vulva (see fibroma pendulum vulvae)

Histologically all types of sarcoma including mixed forms have been described. The great majority are round cell sarcomas Some are spindle cell sarcomas with giant cells Angioblastomas such as hemangio-endothelial or lymphangio-endothelial sarcoma, located on the labia majora are seldom encountered.

Metastatic tumors of the vulvar region may develop in advanced stages of carcinoma of the uterus lungs liver or kidney Special attention has been directed to the metastatic or ectopic" *chorionepithelioma* of the vulva, a rare neoplasm that gives a positive biologic pregnancy test. It may appear as one or several pea to hazelnut sized, circumscribed, dark reddish blue to black protuberances on the vulvar mucosa, located around the introitus and occasionally on the lower vaginal mucosa. The lesions may simulate a circumscribed hematoma or thrombotic varix. These structures show a tendency to spontaneous bleeding and may cause profuse occasionally fatal hemorrhages. A high grade of malignancy and rapid dissemination are characteristic of this neoplasm.

Differential diagnosis: Initial nodular lesions due to vulvar carcinoma will require differentiation from primary syphilitic lesions. Syphilis of all *stages plays an important role in the differential diagnosis of vulvar cancer* For early recognition of malignant vulvar ulcer one must exclude venereal chancre, including chancre mixte secondary and tertiary syphilitic ulcers lymphogranuloma venereum, tuberculosis and, indeed, all other ulcerative and indurative lesions of the vulva. These questions and identical problems have been discussed in the respective chapters as likewise in connection with cancer of the penis For condyloma acuminatum versus carcinoma of the genital region see Chapter 4 for malignancy in leukoplakia and kraurosis vulvae see Chapter 14.

Biopsy is imperative and should be performed immediately in every suspicious lesion of the vulva.

Size consistency tenderness or fixation of the superficial and deep regional *lymph glands* will demand special consideration Tenderness of the glands may be caused by secondary infection of a malignant ulcer The *absence of demonstrable* glandular enlargement is no indication that the malignant process is still localized. Even in advanced carcinoma of the vulva, large compact masses of lymph glands have been known to have

escaped detection in cases in which autopsy has revealed extensive meta static dissemination.

Treatment: Radical surgical procedure, i.e., vulvectomy including radical extirpation of all superficial and deep inguinocrural glands remains the treatment of choice In addition, complete pelvic lymphadenectomy has been advocated by expert surgeons and gynecologists. It is now gen erally agreed that roentgen or radium therapy alone will not suffice. Roent gen irradiation is indicated as a post-operative or palliative treatment. The reader is referred to Savran and associates (*Am J Surg.*, 75 743 1948) and to Allen and Spitz (*Cancer* 6 1 1953)

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CHAPTER 16

NONVENEREAL AFFECTIONS OF THE LYMPHATIC SYSTEM OF THE ANOGENITAL REGION

A. The Lymphatic Drainage of the Genital Region
B. The Nonvenereal Bubo
C. Elephantiasis Lymphangiectatica of the Genital and Anal Region. Lymph Scrotum. Tropical Elephantiasis
D. Ulcus Chronicum Vulvae Elephantiasticum (Esthiomene)
References

A. The Lymphatic Drainage of the Genital Region

The lymphatic drainage of the cutaneous area of the *penis* proceeds from two sets of lymph vessels, namely: (a) a superficial network draining the skin of the shaft of the penis and the prepuce, and (b) a net of deep lymphatics connected with the finely meshed net of the glans penis. Both the superficial and deep lymphatics run into the thick dorsal lymph trunk of the penis, to end in the inguinal lymph nodes above and below Poupart's ligament and, subsequently in the deep lymphatic vessels extending along the iliac blood vessels. There exists also a direct connection of the penile lymph vessels with the iliac lymph glands without a previous passage through the inguinal nodes. The lymphatics of the penis intercommunicate by anastomoses with those of the perineal skin and the neighboring skin of the thighs.

Also the skin of the *scrotum* is drained by lymphatic vessels which communicate with those of the perineal skin they pass along the pudendal vessels to end in the inguinal glands.

Dense communicating nets of lymphatics supply the *labia majora* and *minora*, the hymenal ring and the clitoris. They end in the superficial and deep inguinal nodes and, thereafter or on a direct route, from the vulvar coverings in the iliac lymph glands.

The inguinal lymph nodes receive not only the lymphatics of the genital district but also the major part of the cutaneous lymph vessels of the lower extremities.

B The Nonvenereal Bubo

The nonvenereal bubo develops secondary to inflammatory lesions or to malignant growth in the drainage area of the inguinal glands, or independent of such lesions, as a manifestation of lymphomatous disease

It would only lead to repetition to attempt a description of the great variety of nonvenereal lesions that may cause enlargement of the inguinal lymph nodes. The reaction of these nodes to various diseases of the genital region and a description of the resulting changes have been dealt with in other sections of this book. The present chapter is devoted to a summary of the *diagnostic* problems most frequently encountered in cases with enlargement of the inguinal glands of doubtful origin.

The size, shape consistency painfulness and coalescence of the affected nodes, the presence or absence of suppuration and fistulation, are helpful guides in attempting to differentiate nonvenereal from venereal lymphadenopathy *However in the absence of definite proof of venereal* disease the interpretation of these findings may be difficult.

An important aid in the recognition of syphilitic enlargement of the glands still before the onset of characteristic serologic changes is the demonstration of T pallidae in the aspirated punctate from the glands. This test is useful also in cases of possibly mixed chancre infection or in other suspicious genital ulcers, when dark field examination for T pallidae has yielded negative results

In rare instances, diagnostic uncertainty may be due to the aspect of a perforated *chancroid bubo* As a rule the wormeaten surface of such an ulcer as well as the presence of the Ducrey bacillus will ascertain the *diagnosis*

The moderate slightly painful swellings of the lymph nodes in *gonorrhea* are not likely to present a diagnostic problem. The characteristic changes in the inguinal lymph nodes produced by lymphogranuloma venereum are described in all dermatological textbooks Early recognition will be supported in many cases by a positive Frei test.

The most frequent problems in diagnosis and in the selection of therapeutic procedure are found in enlargements of the inguinal glands in which no residue of some preceding lesion in the drainage area can be found and the history is not suggestive.

It is well known that occasionally patients develop slight to moderate *asymptomatic glandular swellings elsewhere on the body that may persist* for an indefinite period and may defy explanation in spite of repeated general examinations and laboratory tests. Even if restricted to one chain of lymph glands, such enlargement must not be dismissed as irrelevant or attributed to some past unknown inflammation. This pertains especially to unexplained enlargements of the inguinal glands which otherwise are so often involved in venereal, pyogenic or mycotic infections of the genitals.

In his monograph on the *Value of Early Diagnosis of Malignant Lymphomas and Leukemias* (Am. Cancer Soc., No. 7 of a Series on Early Recognition of Cancer 1952) L. F Craver drew attention to the occasionally

unicentric development of *malignant lymphoma* in some chain of lymph nodes. In recent terminology "malignant lymphoma" embraces all variants of Hodgkin's disease and lymphosarcoma (follicular lymphosarcoma, lymphocytic lymphosarcoma, reticulum cell sarcoma) An early recognition of such a condition may enable the physician, if not to cure, at least to relieve the patient temporarily by the use of new therapeutics (nitrogen mus



FIGURE 121 Reticulum cell sarcoma, apparently limited to nodes in the right inguinal chain. (L. F Craver *Value of Early Diagnosis of Malignant Lymphomas and Leukemias*. Monograph, Am. Cancer Society Inc., 1952, p. 31)

tards, cortisone radioactive isotopes if necessary supported by Roentgen irradiation) thus prolonging and rendering more bearable the period of survival.

Craver warns that every unexplained enlargement of the lymph nodes whether local or general, that persists for more than a few weeks, should be regarded as a "danger signal" and therefore renders imperative a skilled examination of the blood, the bone marrow and especially of biopsy specimens. Adequate experience of the pathologist is the promise for an early histological recognition of malignant lymphoma. The differentiation should

include all lesions presenting similar histologic pictures, such as Boeck's sarcoid, tuberculosis, enlargements of the lymph glands secondary to cancer of the prostate penis or testicles.

The role of the lymphatic glands as a possible site of primary malignant neoplasms has been a matter of discussion among pathologists up to recent times. The photograph reproduced in Fig 122 shows the rare condition first described in 1880 by Chambard under the name "*primary carcinoma of the lymph gland.*" Restricted to one gland or one chain of lymph glands it may develop in the neck, axilla or groin. In recent times the *endothelial* nature of this tumor has been established. Many of the reported



FIGURE 122 "Primary carcinoma" of inguinal lymph nodes. (Dermat. Clinic, Univ of Naples, Prof Dr M. Monacelli.)

cases proved at autopsy to be metastatic tumors, derived from a clinically undiagnosed primary neoplasm of the pharynx, tonsil or tongue. Renowned pathologists however were able to confirm the occasional occurrence of such evidently primary endotheliomatous tumors (Ziegler Kaufmann Ewing) Von Recklinghausen tried to differentiate primary and secondary (metastatic) instances Clinically these inguinal tumors were frequently mistaken for tuberculosis. The reader is referred to Ewing, J *Neoplastic Diseases* 4th Ed. (Philadelphia, Saunders, p 335 Chapter on Endotheliomas)

Enlargements of the inguinal lymph glands in *acute infectious diseases* (scarlet fever measles variola, rheumatic fever) usually develop in association with general swellings of the lymph glands. Of particular diagnostic importance is the inguinal bubo in *bubonic plague* which forms immediately after onset of the general symptoms. The bubo rapidly increases in

size, while an initial pustular infection of the lower extremities may remain undetected or may fail to develop into the notorious plague carbuncle. Analogous buboes of the axillary cervical and cubital lymph glands usually follow in the order stated.

As a rule, the plague bubo involves the inguinal and subinguinal glands as well, finally including all deep femoral lymph nodes. The plague



FIGURE 123. Endotheliomatous tumor developing from underlying cancerous inguinal lymph nodes. (Dermat. Clinic, Naples, Prof Dr M Monacelli.)

bubo is extremely painful its contents become hemorrhagic, shining through the stretched skin as a dark red to black tumor Abundant plague bacilli are found in the pus.

There are also less serious nonvenereal infections in which localized lymphadenitis constitutes the apparently primary manifestation In the ulceroglandular form of *tularemia*, the first noticeable symptom is frequently a painful swelling of some group of lymph nodes, the actual pri-

lymph nodes are easily discernible but they may coalesce to form inflammatory tumors with abscess formation

Occasionally the line of progress of the infection along the dorsal lymph cord is well marked by a reddened stripe on the dorsum penis The cord is then felt as a painful thickened lymph vessel Inflammation may persist, even after healing of the initial lesion In excessive lymphangitis of



FIGURE 126. Prurigo Hebrae Note symmetrical swelling of the subinguinal lymph nodes.

the dorsal cord, one or more bulging hemispheric prominences may develop along the thickened, painful lymph cord. Well known as an occasional complication of chancroid, these *bubonuli* develop sporadically also in other bacterial infections of the glans and prepuce Under the microscope pus aspirated from these pouches, will show the causal micro-organisms

Most characteristic is the symmetrical indolent bubo of the subinguinal lymph nodes in *prurigo Hebrae* This condition, rare or little known in the United States is not uncommon in certain parts of Germany Austria and other European countries Prurigo Hebrae is a disease of the poor The

majority of patients of our own observation were pale, undernourished and often scrofulous children living in overcrowded unhygienic quarters

Beginning in infancy and lasting through adolescence up to adult life, continual eruptions of violently itching, minute nodules and small papules spread over the entire body except the axillae and flexor surfaces of the extremities The extensor surfaces, however are markedly affected in the majority of cases. The regional lymph glands of the most involved areas are enlarged (cubital and inguinocrural glands) Also the face, and especially the forehead, may be involved. Excoriations pigmentations, roughness and lichenification of the affected skin, present the characteristic aspect. The skin feels rough, like a grater to the touch. Hebra described the bilateral swelling of the lymph nodes of the inner femoral triangle as a cardinal symptom of this condition, recognizable at the first glance at the undressed patient.

Characteristically the eruptions in prurigo Hebrae often recede spontaneously under ordinary hospital care and proper diet, with or without antipruritic treatment only to recur when the patient is discharged and returns to his former environments.

Swellings and tenderness of the inguinal glands in *herpes progenitalis* have been discussed in Chapter 4.

Treatment: In the majority of cases the nonvenereal bubo represents a complicating condition The treatment of the respective basic affections has been discussed in previous sections. In former times, major surgical procedures, i.e., radical extirpation of the diseased lymph node groups, were widely used in many forms of suppurative lymphadenitis. Thanks to the advances in modern therapy surgical interventions can now in many instances be limited to puncture and aspiration of pus, or to simple incision supported by adequate antibiotic treatment of the causal infection.

Especially in bubo of lymphogranuloma venereum it was customary to perform mass extirpations of the inflamed matted lymph glands, including any adherent tissue Today repeated aspiration of pus combined with drug therapy (especially terramycin and sulfathiazole) and other methods have proved sufficient to control the virus induced disease process in the majority of cases.

Tuberculous enlargement of lymph node groups may recede under properly dosed and filtered Roentgen irradiation The use of Roentgen irradiation in leukemic diseases and lymphosarcoma is thoroughly discussed in textbooks on blood diseases.

In malignant metastatic involvement of the inguinal and subinguinal lymph nodes roentgenotherapy may serve as an ultimate resort in addition to the local irradiation of inoperable carcinoma of the penis prostate and testicles.

C. Elephantiasis Lymphangiectatica of the Genital and Anorectal Region

Lymph Scrotum Tropical Elephantiasis
Schistosomiasis (Bilharziasis) of the Genital Region

Elephantiasis lymphangiectatica is a condition of various origin and not a disease per se. From antiquity to date this term has been used to designate excessive chronic hyperplastic thickenings of the skin and subcutaneous tissue resulting from serious alterations of the lymphatic system with lymph stasis and simultaneous alterations in the blood circulation of the affected area.

Two forms of elephantiasis lymphantiectatica were distinguished in the earlier literature namely "*elephantiasis Arabum*," the so-called "*elephantiasis tropica*" and *elephantiasis nostras* thus separating the exotic forms of elephantiasis from clinically similar but etiologically different conditions occurring in other countries Today the name elephantiasis nostras is obsolete, more especially since in connection with both World Wars tropical diseases causing elephantiasic hypertrophy have been imported sporadically into non tropical countries not infrequently to be mistaken for etiologically different conditions presenting a similar appearance.

Lymph Scrotum

Elephantiasis lymphangiectatica varies widely in appearance and extent When developing in the drainage areas of the inguinal subinguinal and iliac lymph nodes chronic edema, hypertrophy and a continuous suppression of the normal lymph and blood supply eventually lead to gross deformities of the genitals as well as the legs. The scrotum may enlarge to double or triple its normal size or may show such monstrous deformities as observed in tropical filariasis The penis may be embedded between the tumefied scrotal folds In the female, the labia majora and clitoris become hyperplastic and disfigured.

Lymph varicosities may form in elephantiasis as a result of persistent lymph stasis They appear as roundish or irregular prominences in the inguinal region or in the femoral triangle. In elephantiasis lymphangiectatica of the scrotum and less frequently of the labia majora, *lymph vesicles* develop in the edematous cutis, producing pinhead to pea sized, transparent nodules and vesicles scattered over parts of the scrotum or vulva. Bursting readily due to friction and sweating during walking or working these vesicles exude a yellowish white slightly turbid coagulating fluid The oozing subsides during bed rest. Thin crusts cover the remaining erosions Chemically and microscopically one finds a pure lymphorrhea without admixture of chyle

Due to the low resistance of the elephantiasic tissue to trauma and

secondary infection, superimposed inflammation may lead to the formation of circumscribed weeping lesions or ulcers.

Histology: Biopsy of a specimen with closed scrotal lymph vesicles shows (1) the dilated lymph vessels within the surrounding hypertrophic connective tissue accompanied by a lymphocytic, partly perivascular infiltration and (2) the round or oval lumina of the lymph vesicles either



FIGURE 127 Chronic elephantiasic enlargement of the penis due to recurrent erysipelas. (Dermat. Clinic, Naples, Prof Dr M. Monacelli.)

unilocular or communicating to form large cavities. The walls of the cavities are lined by a single endothelial layer Some finely granulated coagula, appearing pale red when stained with eosin are seen within the vesicles. They are intermingled with some lymphocytes.

Etiology: Various factors play a role in the pathogenesis of elephantiasis lymphangiectatica. In tropical elephantiasis, infestation of the lymphatics with *animal* parasites is the causal factor Similar lesions of the lymphatic system with lymph stasis and impairment of the venous blood flow may develop following radical extirpation of whole lymph node

groups or in connection with acute relapsing or chronic infections such as tuberculosis (lupus) lymphogranuloma venereum, destructive ulcerating syphilomas or recurring erysipelas.

As previously explained, modern therapy with antibiotics and sulfonamides has considerably limited the indications for radical removal of infected lymph nodes The control of *erysipelas* by penicillin, aureomycin terramycin, etc. has reduced the incidence of elephantiasic thickenings of the lips scrotum, vulva and other areas, that were formerly so frequently



FIGURE 128. Elephantiasis lymphangiectatica of scrotum and penis showing lymph varicosities and lymph vesicles ("lymph scrotum") (F Callomon *Die Nichtvenerischen Genitalerkrankungen.* Leipzig, 1928 Fig. 58.)

seen as sequelae of recurrent erysipelas. It is particularly in this disease that infection spreads by way of the lymphatics which are crammed with streptococci. The vulnerable elephantiasic skin readily affords a portal of entry for Fehleisen's streptococcus and offers an excellent medium for its growth. Subsequent attacks further enhance the elephantiasic transformation of the tissue

Figure 128 shows elephantiasis lymphangiectatica of the scrotum and penis with single and grouped lymph varicosities, appearing as warty and nodular excrescences and vesicles. Histologically the tissue changes described above were present. The patient, a man of twenty-eight years, presented extensive strangulating scars in the inguinal folds, as sequelae of bilateral radical removal of the inguinal glands.

Analogous cases have been reported in the world literature. Von Berde described elephantiasis scroti in a patient of nineteen years who had previously been operated upon for bilateral colliquative *tuberculosis* of the inguinal lymph glands. Weinberger observed scrotal elephantiasis in a man of twenty-one years of age. In this case "lymph scrotum" had developed without a preceding surgical lymphadenectomy only as a consequence of



FIGURE 129 The same patient as Fig. 128. Histological picture (*ibidem*)

extensive tuberculosis of the inguinal and iliac lymph nodes. On palpation no lymph glands could be detected in the deep folds between the bulging abdominal and inguinal skin

In the female the labia majora are the parts most affected in elephantiasis lymphangiectatica. The labia minora and clitoris are less frequently involved. Scherber described an unusual elephantiasic hypertrophy of the labia minora with densely grouped, tumid elevations and thickening of the upper part of the labia associated with chronic edema of the vaginal introitus.

Tropical Elephantiasis

This condition is caused essentially by filarial infestation of the lymphatic system. The accumulation of adult living and dead (sometimes calcified) filariae within the lymph vessels leads to chronic alterations of the walls obstruction of lymph flow and permanent obliterations When parts of the thoracic lymph duct have been invaded by the parasites, the lymph vessels of the abdominal and pelvic regions become dilated. Chronic lymph stasis and continued spread of the parasites are responsible for the basic tissue changes leading to elephantiasis.

Tropical elephantiasis involves the lower extremities, the scrotum, vulva and the mammae and rarely other parts of the body In the mentioned regions, the disease presents the formerly described deformities in grotesque proportions usually associated with lymph varicosities in the inguinal region or with lymph scrotum, as so often illustrated in textbooks on tropical diseases *The penis may or may not be involved. In many* cases tumefied scrotal skin encloses the penis completely leaving merely a longitudinal groove for the escape of urine Thus, disturbances in micturition develop In the female an excessive hypertrophy of the labia majora may interfere with urination.

The frequent complications of "*filarial abscesses*" is caused by accumulation of masses of dead adult filariae and/or by secondary infection. They *may form anywhere in the affected tissues they occur occasionally in* scrotal elephantiasis Textbooks on tropical diseases give information on additional complications such as hematuria, chyluria, malignant transformation, etc.

Histology: Besides the previously described features of elephantiasis lymphangiectatica, the histological picture in tropical elephantiasis shows extensive worm infestation with inflammatory infiltrations around the infested lymphatics. *Masses of coiled filariae are seen filling the dilated* lymphatics Also the cavities of lymph vesicles may contain filariae. At autopsies calcified dead parasites are often encountered lying free in the tissues There is an excessive proliferation of the connective tissues As a rule a marked *eosinophilia* is found in tropical elephantiasis, not only in the blood, but also as a local eosinophilia in the involved tissues.

Etiology: The causative parasite *filaria* (Wuchereria) *Bancrofti, belongs to the nematodes The females, measuring 0 08 to 0 1 cm.* are longer than the males They are viviparous giving birth to the larvae i.e. minute, highly motile worms (microfilariae) All filariae pathogenic to man require an intermediary host for maturation

The larvae of filaria Bancrofti enter into the bodies of certain mosquitoes (culex, fatigans, et al.) that pick up the microfilariae when stinging

human carriers. Asymptomatic filarial carriers have been repeatedly demonstrated in mass examinations of Pacific populations

Thus animal vectors convey the larval filariae to man. The adult worms developing from the transmitted larvae live on and propagate in the lymphatics, whereas the subsequently produced microfilariae enter the blood stream and circulate in the peripheral blood. They do not mature there, but like the parental filariae, must first pass through an intermediate host.

The tissue changes are not produced by larvae but only by the *adult* worms. However a heavy or repeated infection is necessary to give rise to the terminal elephantiasic deformities described Hundreds of microfilariae are demonstrable in the blood of patients with florid filariasis they appear periodically during the night (microfilariae nocturnae) or less frequently during the day (microfilariae diurnae) The entry of the microfilariae into the blood may be accompanied by attacks of fever

Differential diagnosis: History findings of microfilariae in the blood and biopsy assure the diagnosis in tropical elephantiasis. The diagnosis in elephantiasic deformities secondary to infections of other origin or to wide extirpations of the inguinal glands is self-suggestive. In addition, there occur pseudo-elephantiasic swellings and thickenings of the genitals, in particular of the vulva which must be distinguished from true elephantiasis lymphangiectatica. The borderline between a chronic, stable edema and a beginning hypertrophic process is usually indistinct. Significant by its firmness, however is the massive indurative edema of the vulva occurring occasionally as the initial manifestation of syphilitic infection. It is followed by inguinal scleradenitis. Enlargements of the labia and clitoris following trauma may form as an end-result of an extensive hematoma.

Congenital hyperplasia of the labia majora, labia minora and the clitoris occurs as an individual or familial anomaly and in addition, as a racial phenomenon in certain South African tribes such as the Bushmen Basutos, Hottentots ("Hottentots apron)

Treatment: In the early stages of *filarial* infection prompt evacuation of the patient from the endemic area may suffice to check the progress of the disease in the majority of cases. Spontaneous disappearance of all symptoms has been observed in many such instances (Evans) If removal to a non-endemic country is impossible, careful protection against the vectors by the employment of insect repelling preparations and the use of mosquito nets at night are imperative. Sulfonamides and antibiotics will be of aid in preventing and curing secondary infections in florid cases

The principal factor however namely the complete annihilation of the adult worms still remains a problem for clinical and experimental investigation notwithstanding the promising and sometimes satisfactory

results obtained with various drugs Antimony salts and arsenicals have been found effective in filariasis In particular neostibosan, tartar emetic in freshly prepared solutions, and the antimony salt Fuadin (stibophen) are widely used in tropical filarial disease With the large doses required, however toxic side effects are often inevitable. Hetrazan (Lederle) offers the advantage of oral administration (0.5 to 1 mg after meals three times a day) but has still to pass the test of clinical trial. All details of these methods of treatment and the dosage recommended will be found in the literature on tropical diseases

In tropical elephantiasis of the legs scrotum or other regions, surgical procedures (excisions, plastic operations) may alleviate the patient's handicap by enabling him to move more freely and by reducing the enormous deformities and diminishing their psychological consequences.

Schistosomiasis (Bilharziasis) of the Genital Region

Chronic hypertrophic tissue changes are produced also by infestation with the trematode schistosoma or so-called bilharzia hematobium the parasite responsible for endemic hematuria in Egypt

In this disease, the parasites enter the blood stream of a human victim to inhabit the veins, progressing up into the finest capillaries Subsequently they fill the tissues and organs with the innumerable eggs produced during their life span. Adult worms may live in the blood up to three years. It is the retention of accumulating masses of eggs that produces the characteristic changes in the skin the mucous membranes (especially of the bladder) the cecum liver etc Bladder stones may form around deposits of decayed eggs frequently resulting in pyelonephritis or hydronephrosis. Cancerous transformation of bilharzia tumors of the bladder is one of the most dreaded complications and numerous eggs are then encountered even in the cancerous tissues.

The genital region is a site of predilection for chronic hypertrophic thickenings, papillary and polypoid proliferations in bilharziasis In the *male* extensive inflammatory infiltrations may involve the whole perineoscrotal region, associated with urinary fistulae The penis when involved, is enlarged and distorted, due to scarring periurethral abscesses. Fistulae may be found even on the glans of the penis. For bilharziasis of the urethra, strictures, etc see Chapter 17

In the *female* the labia and the clitoris show elephantiasic thickenings with warty papillomatous or polypoid formations, resembling condylomata acuminata. Also the vagina, cervix and uterus may be involved.

In the majority of cases the first symptom of Bilharziasis noticed is *hematuria* restricted in the beginning to a few drops of blood at the end of micturition. This symptom may recur periodically over years, or may

progress to the excretion of bloody urine (male menstruation in vernacular Egyptian) In other cases, various initial symptoms have been noted, such as *urticarial* and *erythematous* rashes, intestinal disturbances, etc. At this stage the blood eosinophilia is usually already marked.



FIGURE 130 Bilharziasis of penis and scrotum. (Tropen-Institut, Hamburg, Courtesy of Dr Ruge) The case was observed in Kasr-el-Ainy Hospital, Cairo, Egypt.



FIGURE 131. Bilharziasis of bladder and kidneys. (Courtesy of Dr Ruge.)



FIGURE 132. Calcified ova of bilharzia in smear taken from cirrhotic liver (drawing according to Richardson, A. R. *Handbuch der pathogenen Mikroorganismen* V 1 8 Jena, 1913.)

Histology: The most significant finding is the infarct of the tissues with eggs, which is especially marked in bilharziasis of the bladder They are easily detected as oval terminal spined yellowish bodies. Inflammatory infiltrations, capillary hemorrhages, ulcerative degeneration and proliferation of the connective fibers are found in varying degree Exuberant epithelial proliferations are seen in the papillary excrescence

Etiology: The adult female of schistosoma hematobius is about 2 cm long and 0.25 cm broad Larger than the male the fully mature female is found closely attached to the canalis gynaecophorus of the male. The developmental cycle of the parasite has been thoroughly revealed by Leiper (1916) Certain fresh water snails (species bullinus) which are invaded by the larvae, serve as intermediate hosts The larvae do not slip out of the eggs before the latter have been excreted and brought into contact with fresh water or with the urine or feces of patients. The miracidia hatching from the eggs invade the snails only to leave them after having reached the second larval stage As cercerlae, they are then found swimming freely in the water It is the use of such infested water for drinking purposes, or even wading or bathing in it, that exposes human individuals to infestation

Therapy: Treatment with antimony potassium tartrate (tartar emetic) intravenously *remains the most widely used method. After two initial* doses of 2 gr in freshly prepared solutions three injections a week are administered up to a total of 25 to 30 gr (1.5 to 2 Gm.) (Evans) Toxic side effects such as nausea, vomiting, or spasmodic cough, occur in many cases they appear to occur less frequently when sodium antimony tartrate is used in corresponding doses (1 gr per 12 pounds of body weight Evans)

More recently stibophen (fuadin, neoantimosan) and lithium antimony thiomalate have been widely used.

In addition, fistulae polypoid proliferations etc. may demand surgical treatment.

Eggs may be excreted for long periods even after specific treatment dead eggs may remain in the body as irritant foreign bodies. Schistosoma eggs have been demonstrated in Egyptian mummies, proof that schistosomiasis existed at the time of the Pharaohs.

D Ulcus Chronicum Vulvae Elephantiasticum (Esthiomene)

Elephantiasis genito-ano-rectalis and syphiloma anorectal (Fournier) are the terms previously used to designate a peculiar destructive form of torpid anogenital ulcers, leading to elephantiasic changes of the vulva. Originally the term esthiomene had been employed in French nomenclature to designate the destructive form of lupus exulcerans (vorax)

Most frequently observed in older prostitutes, these ulcers were ascribed to preceding gonococcal infections syphilis chancroid with suppurative lymphadenitis, and/or to radical removal of the inguinal glands. In addition, uncleanliness, secondary infection and trauma were believed to favor their development. Severe alterations of the lymph and blood vessels, chronic edema and hypertrophy are common pathologic findings.

The occasional combination with rectal strictures in advanced cases was described already in textbooks of the early twenties of our century. All authors have stressed the stubborn resistance to therapy of this condition. Bacterial findings, if ever present, were found inconclusive.

Etiology: For a long time, Esthiomene had been considered as an autochthonous disease. Today there is no doubt that esthiomene, the so-called ulcus elephantiasticum vulvae, has nothing to do with gonorrhea, syphilis, chancroid, granuloma venereum, tuberculosis or carcinoma. Uncertainty persisted until W. Frei and A. Koppel (1928), Hellerström, and



FIGURE 133. Esthiomene. Elephantiastic transformation of the vulva, tendency to ulceration. (This and the following picture by Courtesy of Prof. F. Pinkus, Berlin.)



FIGURE 134. Chronic edema of the vulva with perianal esthiomene.

other investigators, proved definitely that ulcus vulvae elephantiasticum and its anorectal complications represent a *late manifestation of lymphogranuloma venereum*.

The pathogenesis of anogenital lymphogranuloma was fully revealed after evidence had been collected showing that in the female the primary infection of lymphogranuloma venereum is not infrequently located on the mucous membrane of the vagina and cervix. Progressing through the vaginal wall directly into the perianal and rectal tissues, the infectious process leads to the formation of anorectal lymphogranuloma. Frei tests proved positive in about 90 per cent of all cases. Recent therapeutic achievements have opened the way for an effective treatment.

Figures 133 and 134 give a good idea of the clinical aspect of esthio-

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Figures 133 and 134 give a good idea of the clinical aspect of esthio-

mene due to anogenital lymphogranuloma. There are bluish red to brownish, smooth or uneven, rather firm, thickenings and bulges associated with papillomatous proliferations on the labia, the clitoris and vaginal introitus Very soon erosions fissures and solitary or multiple ulcers develop chiefly between the tumefied folds of the mucosa. The base of the ulcers is even with little tendency to granulation the borders are rolled inward, and are usually callous

These changes may exist for a long time, or may slowly extend to the urethral meatus and at the same time may progress to the anorectal region There the same changes are produced, with turbid swellings of the rectal mucosa, ulceration cicatrization and stricture formation As a rule these strictures are located in the lowest part of the rectum, not very distant from the anal orifice (for literature see Beerman)

Painful destruction of tissue may result, complicated by anorectal sinuses and rectovaginal fistulas Scarification and hypertrophy result in distortions and dislocations of the urethral meatus and introitus On inspection it may be difficult to find the meatus within this labyrinth of folds proliferations ulcers and erosions

An insidious protracted course is the rule However to some extent, spontaneous retrogression may occur although rarely before some years have passed. During pregnancy and the puerperium a more rapid course has been observed.

Histology: The lymphotropism of the lymphogranuloma venereum virus explains the characteristics of the histological picture Inflammation, dilatation and obliteration of the lymph vessels are most obvious often associated with periphlebitic changes ulceration and chronic hypertrophy of the connective tissue highlight the principal symptoms Occasional giant cells described by Casper proved to be different from the Langhans giant cells There are no tissue changes elsewhere suggesting tuberculosis

Differential diagnosis: The recognition of vulvar and anorectal lymphogranuloma is not difficult in advanced cases even in the absence of other manifestations of the virus disease It may be more difficult in initial stages of esthiomene especially in prostitutes who are so frequently exposed to venereal infections. The possible coincidence of late *syphilitic* ulcers with lymphogranuloma venereum can not be excluded, neither positive results of Frei tests nor those of serologic syphilis tests are decisive under the circumstances It is known that tertiary destructive ulcers of the anogenital region occasionally produce pseudoelephantiasic changes In these instances an early examination of the rectum (rectoscopy) may reveal anorectal changes as possible precursors of stricture

Biopsy will be helpful in doubtful cases and is imperative to exclude a *malignant* ulcer formation.

The slow development, chronicity absence of pain, and in unrecog nized cases, resistance to therapy distinguish esthiomene from *chancroid*. Ulcers derived from fungus infection (sporotrichosis) when limited to the anogenital region can be identified by demonstration of the causal fungus

Treatment: The vulvar and anorectal lymphogranuloma respond to the various methods of treatment employed against the basic disease. Anorectal sinuses and rectovaginal fistulas demand surgical treatment or may require plastic operations in the presence of extensive elephantiasic deformities.

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PART III

CHAPTER 17

NON-GONOCOCCAL (NONSPECIFIC) URETHRITIS

A. Introduction
B. Non-gonococcal Urethritis Caused or Probably Caused by Bacterial Infection (Urethritis Bacterica)
C. Urethritis Non-gonorrhoica Chronica (Waelsch) Virus Induced Urethritis
D. Urethritis Caused or Probably Caused by Protozoa and Flagellatae
E. Urethritis Mycotica
F. Urethritis in Relation to General Diseases
G. Urethritis Associated with Neoplasms of the Urethral Wall
H. Urethritis Due to Mechanical, Thermal and Chemical Lesions of the Urethral Mucosa
I. Non-gonococcal Infection of Accessory Canals of the Urethra or of Congenital Canals and Cysts of the Genitoperineal Raphe
J. "Nonvenereal" Strictur of the Urethra
K. Non-gonococcal Discharg in Children
References

A. Introduction

The term *"non-gonococcal"* or *"nonspecific" urethritis* (*urethritis non gonorrhoica*) does not refer to a single well characterized disease, but is commonly used to designate a large group of morbid processes of very different origin

This great diversity of etiological factors stands in sharp contrast to the monotonous features of the clinical picture, including urethral discharge of varying quantity consistency color and duration. As a rule, the clinical manifestations are milder than those produced by gonococcal infection. Differentiation from chronic gonorrhea, or "postgonorrheal urethritis may however present an intricate problem. Every available means must be used to exclude a possible gonorrhea, but there are cases in which a definite diagnosis is impossible.

The history of a patient with non-gonococcal urethritis is only of limited value The history of earlier gonorrhea would not exclude the possibility of a subsequently acquired nonspecific urethritis. Many cases of urethritis non-gonorrhoica have nothing to do with venereal infection they may develop independently of any sexual contact. Other forms are due to general diseases. Chemical and mechanical irritation toxic agents, diseases of the upper genito-urinary tract and pathologic changes of the urethral wall may play a role in the pathogenesis of nonspecific

urethritis Recent investigators have dealt in particular with the relation of urethral discharge to general diseases

Although some forms of non gonococcal urethritis are very uncommon, the majority are anything but rare. Today the diagnosis and treatment of non-gonococcal urethritis belong to the duties of the general practitioner as well as to the urologist.

Various attempts have been made to classify the different forms of non gonococcal urethritis It appeared logical to subdivide the cases into those of bacterial and non bacterial origin. However it is too frequently impossible to confirm the specificity of the micro-organisms demonstrated in smears or identified by culture many of which do not belong to the common bacterial flora of the urethra. Neither the total, or almost total absence of bacteria in smears will permit definite etiological conclusions. Non bacterial forms (the uréthrites aeptiques or microbiennes of French authors) have received more attention since recent research revealed the possible relation of urethritis chronica Waelsch to virus infection.

As previously mentioned, a strict classification into venereal and nonvenereal types cannot be maintained. A more satisfactory grouping would be a division into primary and secondary urethritides (Frühwald, Cave) i.e into conditions caused by localized infection and other lesions of the urethral mucosa and those occurring as a symptom of general disease To some extent, all classifications may appear incomplete

In harmony with the particular purpose of this textbook, the incidence and practical significance of the various forms of non-gonococcal urethritis have been major determinants *in the organization of this* chapter

B Non-gonococcal Urethritis Caused or Probably Caused by Bacterial Infection

(Urethritis Bacterica)

Cardinal Symptoms

Short incubation period (two to four days) acute onset, slight to moderate discharge of watery mucous or mucopurulent consistency either transparent, or of milky grayish to yellowish appearance urine clear or slightly turbid, with or without threads slight or no complaints rarely exceeding a burning sensation on micturition constant or predominant microscopic evidence of some type of micro-organism, occasionally intermingled with the usual urethral bacteria.

Sometimes discharge is restricted to a tiny watery morning drop Nonspecific urethritis in the male may be so trivial as to escape attention in every day life. In other cases the discharge increases considerably during

the first week. Clinical symptoms are mild, as a rule and not to be compared with those of acute gonorrhea.

The condition runs a course of about two weeks However there are exceptions. Occasionally complications, such as involvement of the posterior urethra, prostate or epididymis, similar to those caused by gonococcal infection, may prolong the disease Instances have been reported of nonspecific peri and paraurethritis, arthritis and very rarely of iritis and iridochoroiditis (von Wahl, Waelsch, Baermann, Fiser *et al.*)

Waelsch observed a case of pseudodiphtheritic infection restricted to a paraurethral duct in a patient with hypospadia. Fiser observed a severe cavernositis complicating primary coli-urethritis in a twenty-one year old patient, who allegedly had never had sexual intercourse. In this case the infection was derived from the phimotic prepuce.

Generally *prognosis* is favorable in nonspecific urethritis and there are no serious social implications like those connected with gonococcal infection.

Etiology and Pathogenesis

Our etiological knowledge is far from complete The number of microorganisms supposed to cause primary bacterial urethritis is legion. The literature contains reports on urethritis due to streptococci or staphylococci, enterococci, B coli commune, pneumococci, diplococcus pneumoniae, bacilli of the pseudodiphtheria group B influenzae streptobacilli, B crassus, B tetrogenes sarcine bacteria, etc. In recent American and English literature, the etiological significance of pleuropneumonia like organisms has been stressed.

In checking the literature, many contradictory findings will be encountered. The interpretations offered in numerous case reports of the past did not withstand critical objections regarding the specificity of bacteria found in the discharge. However in many instances, the pathogenicity of the respective bacteria has been confirmed A classical example is Bockhardt's *staphylococcic urethritis*. This author succeeded in transmitting staphylococci, isolated by culture from the urethral and vaginal discharges of man and wife, to the urethral mucosa of a normal individual. Similar results have been obtained by Baermann in urethritis caused by *pseudodiphtheria* bacilli, in one instance the urethral infection was followed by epididymitis with bacilli in the aspirated fluid. Later bacilli of the pseudodiphtheria group were demonstrated in nonspecific urethritis by Lipschütz, Mracek, Schaeffer Ullman, and recently Salaman.

Von Wahl emphasized the pathogenic role of *streptococci* at the same time drawing attention to the frequency of streptococci in symbiosis with gonococci. Radaeli was able to demonstrate a urethritis of gram-negative

streptococcic origin Felke found lactic acid forming streptococci causing urethritis the organisms have been isolated from husband and wife Special studies have been devoted to the etiological role of *enterococci*. These round or elongated micro-organisms uncommon in urethral or vaginal discharge, are related to the streptococci. (They may occur intracellularly in pairs, like gonococci, or in chains or irregular groups.) The discharge is of a muddy grayish appearance and less viscid than that of chronic gonorrhea (Lavenant, Trifu, Dreyer) Trifu found specific vaccine therapy effective in enterococcal urethritis Urethroscopy revealed a moderate hyperemia, follicular inflammation and desquamation of the mucous membrane.

Brünauer described *sarcine urethritis* with marital contagion and frequent relapse in both partners which responded to specific vaccine therapy Sarcine organisms were a constant finding in smears from both man and wife Sarcinuria is not uncommon in diabetics (A. Abraham)

One form of urethritis, apparently unknown in the United States but quite common in tropical countries (especially in Egypt) is caused by the gram-negative coccobacillus *la pasteurella* Usually this micro-organism causes a general disease, resulting in pleuropneumonia, empyema and para myositis. Urethritis may appear as a symptom due to the general spread of the infection ("Pasteurellose uréthrale, described by Papadopoulo-Syngellakis Petzetakis) *Primary infection of the urethral mucosa*, causing urethritis, has been reported but remains doubtful, even though pasteurella occurs as a saprophyte of the normal urethra, in tropical countries The condition is characterized by a profuse, purulent discharge and is frequently complicated by orchiepididymitis and fever Coccobacilli are present in smears and urinary threads and occasionally also in the prostatic secretion and sperma.

The problem of coli-urethritis demands special attention. Although coli infections of the urethra are usually transmitted from the upper urinary tract, primary coli urethritis, without involvement of other portions of the urogenital system has been described in several convincing cases (Finger Fiser Klausner Pezzoli *et al.*) Following an incubation period of three to four days, a profuse discharge develops rapidly The orificial area is swollen. Fever purulent or slightly bloody discharge, prostatitis and epididymitis complete the clinical features.

The pathogenic importance of findings of *pleuropneumonia-like organisms* (L-organisms") in bacterial urethritis is still under discussion. Pleuropneumonia organisms are well known as causal agents of animal disease producing pulmonary edema, exudative pleuritis and polyarthritis in cattle, sheep goats, etc. Recently similar organisms have been identified in the urethral prostatic, vaginal and cervical discharges of human beings often

in association with other bacteria (Harkness *et al.*, 1948) Their transmissibility from the one to the other partner in young married couples has been described. Willcox and Findlay reported disappearance of these organisms and of discharge after aureomycin treatment. Reports still appear too scarce to draw definite conclusions concerning their specificity

The reader is referred to recent investigation on the rôle of pleuropneumonia like organisms in the urogenital tract of men and their possible pathogenic action, alone or in symbiosis with other microorganisms, published by H Röchl, Th Nasemann and E. Stettwieser in *Hautarzt* 25:340–347 1954. In this paper also the difference between these organisms and the so-called L-forms are discussed.

Route of Infection

Judging from the literature, bacterial infection of the male from the female partner is common. Bacterial urethritis may also be transmitted independent of direct contagion from one individual to another as for instance by careless catheterization and the use of imperfectly disinfected instruments, or by deliberate introduction of foreign bodies.

Spirochetes in nonspecific urethritis: Castellani was one of the first to direct attention to the occasional occurrence of spirochetes in the normal urethra (treponema urethrale, Castellani) Constant findings in a purulent discharge with none, or only a few insignificant bacteria have been reported by Castellani and by Bacigalupo The latter author succeeded in isolating a spirochete of high motility in a mucopurulent discharge of a male patient. This chronic discharge subsided after treatment for four days with a novarsenobenzol solution, increasing in concentration from 1 to 10 per cent. The scarceness of reports does not permit definite conclusions concerning the specificity of such findings.

Differential Diagnosis

Three cardinal factors are essential to arrive at a well established diagnosis in bacterial nonspecific urethritis (1) differentiation of bacterial urethritis from chronic gonorrhea (2) differentiation of the various forms of bacterial urethritis from each other and (3) proof of the specificity of the suspected micro-organism in the case being examined.

As explained in the introduction to this chapter the patient's history is of limited value All clinical and laboratory methods must be employed and repeated over a long period of time to exclude gonococcal urethritis. Culture methods should be employed to confirm microscopic findings. Provocative methods should not be neglected.

It may be difficult, if not impossible to prove that the suspected micro-organism is actually the pathogenic agent in a given case. The model

experiment of Bockhardt, cited above in transmission of staphylococcal urethritis, has demonstrated one method for establishing definite diagnosis. However in practice the experimental transmission of the infection from one man to another could hardly be employed as a diagnostic method. In many instances, the clinical examination of both partners will offer a solution to the etiological problem.

One of our own patients a married engineer was surprised by the onset of an annoying discharge two days after marital intercourse. Dense masses of gram negative bacilli were found in the smears from the husband and in scrapings from the vaginal mucosa of the wife. Recovery followed

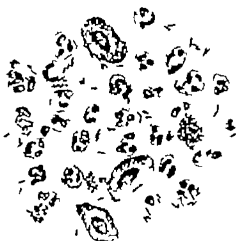


FIGURE 135 Smear from nonspecific bacterial urethritis. Identical bacterial findings in wif and husband, without concomitant microorganisms (This and Figure 136 from hand drawings of Dr C.)

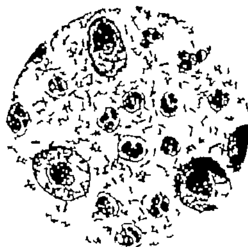


FIGURE 136 Smear from urethritis post gonorrhoica, abundant mixed bacterial flora

three weeks of mild local treatment. Following three months of sexual abstinence, the urethritis recurred immediately after resumption of marital relations This time recovery followed two and one half weeks of treatment There were no symptoms of urethritis or colpitis in the female partner and no history of venereal disease in the husband.

Treatment

Despite the progress of etiological research, the therapy of nonspecific urethritis has remained unsatisfactory Irrigations or injections of solutions of antigonococcal chemicals are of limited value and may rather cause additional irritation of the mucous membrane Occasionally injections of potassium permanganate solution (0.05 to 0.001) or of zinc sulfate solu-

tion (0.5 to 0 1 per cent) or resorcinol solution (0.5 to 1 0 per cent) two or three times a day may suffice to cure the condition. Recently E L. Morgan found instillation of acriflavine (1 to 1000) once or twice daily for seven days, effective in patients with urethritis non-gonorrhoica. However it must be kept in mind that certain cases of bacterial urethritis show a tendency to heal spontaneously As a rule improvement is transitory and relapses occur frequently after purely local treatment.

Sulfonamides: Today irrigations or injections are used only in combination with internal administration of *sulfonamides* As in gonorrheal urethritis, so also in certain cases of bacterial urethritis sulfonamide compounds have proved effective. However the number of good results is considerably smaller than that obtained in gonorrhea. Sulfonamide therapy is of greater importance in the treatment of chronic urethritis of the Waelsch-type

Penicillin is of little value in nonspecific urethritis as compared with its remarkable effects in gonorrhea. Parkhurst, Harb and Cannefax, in checking two thousand eight hundred and twenty-one cases of male and female gonorrhea, encountered not a single instance in which an adequate dose of penicillin did not render the patient culturally free of gonococci. They concluded that discharges which fail to respond to penicillin, are not of gonococcal origin. Failure of penicillin rather indicates the presence of a nonspecific urethritis. For this reason, *a test injection of penicillin* may be of aid in differentiating nonspecific urethritis from gonococcal infection

Other antibiotics than penicillin have a powerful effect in bacterial urethritis. The selection of the proper antibiotic in a given case depends on the type of the suspected bacteria, its reaction to gram-staining and its cultural behavior

Streptomycin has yielded excellent results in cases of urethritis caused by staphylococci or bacteria of the pleuropneumonia group (Pulaski, Kane and Foley Willcox, *et al*) Willcox obtained prompt response to a single dose of 0.2 to 1 0 gm. of streptomycin. In the cases reported, there was a profuse discharge, hazy urine and in one case epididymitis. In each instance, improvement was spectacular Two of the four patients had relapses, but were cured by a repetition of streptomycin treatment.

Aureomycin: Encouraging results have been achieved in various forms of bacterial urethritis with *aureomycin*. Aureomycin hydrochloride may be given by mouth in capsules of 250 mg. Aureomycin is active against staphylococcus, pneumococcus streptococcus fecalis pleuropneumonia organisms and gonococcus Finland and his associates recorded complete cure in forty-nine of sixty-six cases of gonorrhea and in two cases of non-gonococcal urethritis which had previously failed to respond to penicillin streptomycin and sulfonamides Pleuropneumonia bacteria were found in

the discharge of one of these two patients The total dose required was 9 gm. of aureomycin given orally over a period of nine days and 11 gm. over a period of fourteen days respectively Willcox and Findlay treated four patients by the method recommended by Collins, Finland and Paine. A total of 1 000 mg of aureomycin was administered to three of these pa tients and a total of 2,000 mg to the other patient, over periods of twenty four to fifty hours Three of the patients responded perfectly the fourth patient suffered a relapse but was cured by a second aureomycin treatment.

Other Antibiotics: Also other new antibiotics may be used with similar beneficial effect as for instance *chloramphenicol* (1 gm. three times a day for two succeeding days Chen & Dienst) or *terramycin*. *Terramycin* proved effective in urinary tract infection including nonspecific urethritis in other wise refractory instances Its low toxicity has been emphasized (McKenzie and Nugent) initial dose 2 gm 1½ gm., on the second day followed by 1 gm. daily for three to four days up to a total of 7 gm. In a more recent study Willcox (*Brit J Vener Dis* 29 225 December 1953) compared the results obtained after treatment of 460 patients with nonspecific urethritis given sulfonamides, penicillin streptomycin, chloramphenicol, aureomycin and terramycin The three most successful drugs were terramycin, aureomycin and chloramphenicol in the order stated, terramycin thus being the best drug of these tests The optimum dosage of terramycin was in the region of 2 gm daily given for five days.

In certain types of bacterial urethritis, *autogenous vaccine* therapy has proven to be successful and especially in coli urethritis This treatment should be reserved for cases that resist other therapeutic methods

C Urethritis Non-gonorrhoica Chronica (Waelsch)

Virus-Induced Urethritis — Urethritis Chronica (Waelsch) in the Light of Modern Virology

Virus-Induced Urethritis

In 1901 L. Waelsch contributed a classical description of a particular form of infectious urethritis well defined by its clinical features and its chronic course Although symptoms may vary to some extent, and might seem to fit a number of different kinds of nonspecific urethritis the type "*urethritis chronica Waelsch* has been established as a clinical entity This condition is not too rare. It may confront the physician with difficult diag nostic and therapeutic problems The original description of Waelsch has remained valid to the present time.

Cardinal symptoms: The cardinal symptoms are (1) a rather long incubation period (five to sixteen days) (2) slight subjective symptoms (3) marked chronicity and (4) resistance to therapy

The discharge is slight to moderate in amount and is frequently restricted to a watery or mucous morning drop of gray or yellowish color Occasionally the discharge may be somewhat tough or mucopurulent. The urine is either clear or hazy with heavy threads and shreds. Uncharacteristic bacteria are scanty or completely absent.

This condition may persist over months and years, with slight remissions and exacerbations. Complications are not as uncommon, as it may appear from the reports of the literature. Occasionally epididymitis develops but with symptoms milder than in bacterial epididymitis. Also a mild prostatitis may occur A large number of patients with Waelsch's urethritis have never had gonorrhea. The infectious nature of the condition has, however been clinically ascertained.

Judging from the literature, only infections of the male partner have been reported, the female partner presenting no clinical symptoms. Galewsky made the significant observation of two men infected by the same woman. On the other hand, men who suffered from Waelsch's urethritis, have married without evidence of a subsequent infection of their wives

Notwithstanding the relatively mild character of this affection, its chronicity and resistance to therapy may drive a neurasthenic patient to despair

The designation "urethritis non-gonorrhoica, Waelsch" should be restricted to cases that present unequivocally the cardinal symptoms described by Waelsch. Some authors have objected that similar symptoms may develop also in the course of other untreated non-gonococcal catarrhs. Waelsch repeatedly emphasized the significance of a long incubation period and of the consistency of the discharge which may be watery or gray to yellowish gray or in other cases more viscous, but never abundant.

Glingar (1914) added characteristic *urethroscopical findings* to the symptomatology of this condition, including (1) a reddened mucosa of the anterior portion of the urethra, and (2) a circumscribed or diffuse infiltration of the involved mucosa, associated with distinct, somewhat translucent *gray or yellowish nodules of the size of millet seeds* or pinpoints, similar to the nodules characteristic of trachoma. Waelsch, however did not consider that the absence of such nodules in the urethroscopic picture would necessarily refute the diagnosis of urethritis Waelsch, in otherwise typical instances.

Etiology: Still, at the end of World War I the etiology of urethritis chronica (Waelsch) was veiled in obscurity Opinions differed, as to whether this condition is contagious and therefore is transmissible from individual to individual by intercourse The momentousness of this question in premarital examinations is evident.

Progress of cell research and the introduction of the electron-microscope paved the way for a better understanding of abacterial urethritis and similar infections

Urethritis Chronica (Waelsch) in the Light of Modern Virology

Halberstaedter and Prowaczek (1907) were the first ones to find inclusion bodies in cells of urethral discharge from patients with abacterial urethritis, i.e. basophilic cell inclusions analogous to those previously found in trachoma and in an abacterial form of conjunctivitis known today as inclusion blennorrhea of the newborn." All these inclusion bodies had been interpreted as possible products of a virus infection. Further progress of cell research, especially Lipschütz findings of elementary corpuscles within the inclusion bodies, corroborated this assumption. The hypothesis was established that the inclusion bodies (the chlamydozoa of Halberstaedter and Prowaczek) harbor the virus itself (the Elementarkorperchen or strongyloplasms" of Lipschütz)

The presence of inclusion bodies in cases of abacterial urethritis was confirmed by numerous investigators (Siebert, Scherber Lindner Thygeson, *et al.*) Similar cell inclusions were detected also in many instances of lymphogranuloma venereum (Gay Prieto Findlay Miyagawa, Hellerström) As is generally known the initial manifestation of lymphogranuloma venereum can appear either as a localized ulcer or nodule, or as a nonspecific urethritis before the development of the inguinal bubo and other symptoms.

Experimental research and the use of the electron microscope substantiated the virus etiology of a large group of hitherto unexplained diseases, including trachoma, inclusion blennorrhea of the newborn molluscum contagiosum common warts herpes simplex and lymphogranuloma venereum.

Fundamental factors point at a *possible etiological relationship* between lymphogranuloma venereum, trachoma, inclusion blennorrhea and urethritis chronica (Waelsch)

In spite of their clinical disparity those affections seem to represent closely linked diseases (Harrison and Worms) The hypothesis gained ground that the virus of Waelsch s urethritis may be closely related to if not identical with the virus of lymphogranuloma venereum. This problem, however is still under discussion

In favor of the assumption of a common or related causative agent speak the following facts

(1) Frei's intradermal reaction, characteristic of lymphogranuloma venereum rendered positive results also in numerous cases of Waelsch s urethritis.

(2) Frei and his associates were able to provoke positive reactions in patients with lymphogranuloma venereum after intradermal injection of an antigen prepared from discharge of urethritis-Waelsch.

(3) Sulfonamide compounds and antibiotics which are surprisingly effective in many cases of the above named ocular affections and lymphogranuloma venereum, proved to be likewise effective in typical cases of Waelsch's urethritis (Harrison and Worms, Willcox, Chen and Dienst, Meenan, *et al*)

Objections have been made as follows

(1) Bizzozero and Midana obtained positive Frei reactions in fifteen out of eighteen patients with Waelsch's urethritis. These investigators inclined to believe that the majority of cases of urethritis of the type Waelsch might, in fact, be lymphogranuloma urethritides. It should be objected that up to the present time subdural inoculation of mice with discharge from urethritis Waelsch did not produce meningoencephalitis, like that observed following inoculation with lymphogranuloma material.

More recently Midana, in association with Murtula resumed these studies in another series of patients with non-bacterial chronic urethritis In 45 per cent of all cases, a strongly positive Frei reaction was stated. The authors suggested that possibly the symptoms of Waelsch's urethritis may be elicited by various viruses including the virus of lymphogranuloma venereum.

(2) Gay Prieto (1951) noted that in nineteen cases of urethritis-Waelsch which he observed over a period of several months, he never saw an inguinal bubo suggestive of lymphogranuloma venereum. In accordance with this statement, we must admit, that likewise no one of our own patients with typical urethritis chronica (Waelsch) did ever show a lymphadenopathia of the lymphogranuloma venereum type.

Macrae and Willcox (*Brit J Vener Dis.* 29·231 1953) performed 410 complement fixation tests with a lymphogranuloma venereum antigen on 141 patients with nonspecific urethritis or their female consorts and in addition, on 132 controls. This investigation failed to establish any significant relation between viruses of the psittacosis-lymphogranuloma venereum virus antigen and patients sera.

(3) There are still differences of opinion regarding the specificity of the Frei reaction, since occasionally positive reactions have been noted in cases of psittacosis or pneumonitis. It should not be excluded that occasionally also an antigen prepared from discharge of urethritis Waelsch may elicit such unspecified reactions.

Special attention has been directed to the fact that abacterial urethritis showing all characteristics of the Waelsch-type promptly responded to sulfonamide treatment in elaborate clinical trials performed by Harrison

and Worms This statement apparently corresponds to similar therapeutic effects of sulfonamide compounds and especially of sulfathiazole in lymphogranuloma venereum, observed in human beings as well as in inoculated animals In a comparative study on chemotherapy of lymphogranuloma venereum in mice we saw that sulfathiazole, especially recommended for certain clinical forms of the human disease, proved most effective also in experimental lymphogranuloma Further investigation is necessary to confirm these statements

Reservation is advisable when evaluating instances of Waelsch s urethritis combined with *conjunctivitis* In two cases observed by Thygeson and Stone, inclusion bodies were demonstrable only in the urethral discharge but never in the conjunctival pus Purely clinical statements, without the demonstration of inclusion bodies do not allow definitive conclusions

Important observations, however point at a possible close relationship between trachoma, inclusion blennorrhea and urethritis Waelsch.

Basophilic inclusion bodies have been demonstrated in the cervical discharge from mothers of infants presenting the neonatal form of inclusion blennorrhea. Infection of the newborn infant must, therefore have occurred during its passage through the birth canal Repeatedly inclusion bodies have been detected also in a mild urethral discharge of fathers of *such infants*

Of special significance are the following observations (1) Lindner (1910–11) observed a patient with early trachoma, who was suffering from urethritis of the type-Waelsch, (2) Thygeson and Stone (1942) the only children of two physicians showed inclusion blennorrhea shortly after birth. Three and one half years before the father of the one infant had contracted urethritis-Waelsch. The father of the other infant had never *before such urethral affection, but acquired Waelsch s urethritis* soon after return of his wife from the hospital (3) F Hamburger (1934) two children of another family born at an interval of two and one-half years, showed blennorrhea soon after birth, the father presenting no symptoms of urethritis, and (4) Julianette and Lange (1938) an analogus observation in two newborn infants, born at an equal interval

These observations indicate, that mothers of infants with inclusion blennorrhea may harbor the dormant virus for a long time Harrison and Worms suggested that certain otherwise unexplained cervical and urethral catarrhs may be due to virus infection This assumption is supported by occasional findings of inclusion bodies in scrapings from the cervix of women with cervical catarrhs.

Also in other forms of conjunctivitis, inclusion bodies have been demonstrated especially in the so-called "swimming bath-conjunctivitis (Thygeson and Mengert) It is however uncertain whether the causative

virus is identical with, or is related to that of inclusion blennorrhea of the newborn.

Our review will suffice to display the complexity of the problems remaining for further investigation.

Differential diagnosis: Pronounced chronicity mild clinical symptoms from the beginning, a slight to moderate watery or mucopurulent discharge and the absence of bacteria or at least, of any characteristic bacterial flora in the smears, differentiate Waelsch's urethritis from other forms of nonspecific urethritis. Differentiation from chronic gonorrhea is of first importance and should be based upon prolonged microscopical observation, culture and provocative tests. Occasionally when chronic gonorrhea cannot be definitely excluded even after having exhausted all known diagnostic procedures, the effect of penicillin shots may render an auxiliary method for the distinction of urethritis Waelsch from chronic gonorrhea. The definitive disappearance of previously uninfluenced chronic discharge following penicillin shots points to a gonococcal condition rather than to a nonspecific urethritis.

Theoretically it may appear important to search the discharge in each uncertain case for inclusion bodies (Harrison and Worms) However such a procedure will, for practical reasons, have to be reserved for clinical research.

Treatment: Until quite recently urethritis of the type-Waelsch has been regarded as particularly resistant to treatment. All earlier methods seemed doomed to failure and many patients finally became resigned to no treatment.

Prospects for a rational therapy for this condition appear brighter now however since its close relationship with certain virus diseases has been disclosed. Opinion prevails that Waelsch's urethritis responds promptly to sulfonamide treatment. This is in agreement with the clinical results of sulfonamide treatment in cases of lymphogranuloma venereum and inclusion blennorrhea. For this reason, sulfathiazole or sulfadiazine should be employed in doses similar to those used in the therapy of gonorrhea.

The efficacy of antibiotics and especially of aureomycin in the treatment of virus-produced urethritis has been recently emphasized. Clinical trials seem to indicate that aureomycin, orally renders similar beneficial results in Waelsch's urethritis as obtained in cases of lymphogranuloma venereum As in lymphogranuloma venereum, a dose of 250 mg of aureomycin four times a day given for one to two days, has been recommended (Garvin Sikorski, Gay Prieto *et al.*) Dramatic response to aureomycin treatment was reported by H. Sikorski (1951) in fourteen cases of Waelsch's urethritis. Chen and Dienst obtained a definite cure in a patient with urethritis-Waelsch by administration of chloramphenicol for two days in doses of 1 gm. three times a day This patient had suffered numerous

relapses in past years The value of terramycin and other new broad spectrum antibiotics in the therapy of Waelsch s urethritis is still under discussion. A definite evaluation of antibiotic treatment in urethritis chronica (Waelsch) will not be possible before the results of large scale trials can be colligated.

D Urethritis Caused or Probably Caused by Protozoa

Amebic Urethritis Trichomonas Urethritis

Amebic Urethritis

The findings of amebae in urethral discharge brought up the question as to whether protozoa are capable of causing a local infection restricted to the urethral mucosa. The paucity of reports on this question renders an answer difficult. In certain cases of *amebic dysentery* a purulent urethral discharge has been observed in which entamebae were found constantly in wet and stained smears occasionally in the prostatic secretion and as a rule, in the sediment of centrifugated urine Petzetakis for instance described *amebic urethritis* with purulent discharge and terminal hematuria in acute amebic dysentery He observed urethral discharge with amebae even in dysentery patients *without* actual *intestinal symptoms* Hines, on the other hand, noted discharge without any findings of amebae during acute dysentery attacks while at the same time amebae were found in the stools and occasionally also in the sperma. In these instances, discharge subsisted promptly under emetine treatment as did the intestinal symptoms.

Amebic contents in the urine have been observed for a long period, following healing of the general disease. Rocca found cystic and vegetating forms of entameba histolytica still present in the urine two years after clinical cure of the intestinal disease, in a patient who had acquired dysentery during World War I

Trichomonas Urethritis

Special attention should be directed to *trichomonas urethritis of the male* This condition the object of clinical and experimental studies for a long time, now appears to be well established as a special type of non specific urethritis. It is possibly not quite as rare as might be judged from the literature Although there still remain some divergences of opinion there is little doubt that trichomonas a common parasitic inhabitant of the female genital mucosa, and a frequent cause of chronic vaginal dis charge can be transmitted to the male during intercourse and cause urethritis. The urethritis thus produced in the male shows the same tendency to chronicity and relapse, which is characteristic of female trichomoniasis.

The presence of trichomonas in the vaginal discharge does not necessarily imply sexual contagion. Quite frequently gynecologists encounter trichomoniasis in unmarried virginal women. Flagellatae, very similar to trichomonas vaginalis, have also been found in the human intestine. Since the specificity of the vaginal flagellata has not been definitely proved, this may afford a reasonable explanation of the mode of infection in the female (F L. Lydon)

Trichomonas may appear in the male urethra only as a parasitic invader In other instances, the trichomonas infection may be superimposed on a pre-existing bacterial urethritis. In this manner the flagellata may act as a pathogenic agent in symbiosis with some type of bacterium. Usually however trichomonas findings in the male are not associated with any constant bacterial flora and they have frequently been demonstrated in an otherwise sterile discharge. Occasionally urethritis was found associated with chronic prostatitis and with flagellatae in both the urethral and prostatic secretion.

Clinical symptoms: Trichomonas urethritis in the male is characterized by a long incubation period (four to six weeks) The onset is marked by an itching and burning sensation which is soon followed by a discharge, varying in amount, consistency and color The course is chronic, with remissions and exacerbations. The discharge may be watery milky or mucopurulent. The first portion of the urine is more or less turbid, with heavy threads and shreds. The bladder is rarely affected. Numerous flagellatae with some epithelial cells and a moderate number of leucocytes are seen in the wet and stained smears. Flagella are visible in dark field examinations, especially after the addition of a drop of Lugol s solution. With this method, also the marginal undulating membrane becomes visible.

During a long observation period, the organisms may disappear for a time, but will reappear after several weeks or months. Such resting phases should not be mistaken for a cure The temporary disappearance of trichomonas has been observed also in female trichomoniasis. As a rule infection in the male is due to sexual contagion. On the other hand, infection of the female from a trichomonas urethritis in the male has not been described in the literature Such a possibility cannot be denied, however

The flagellata trichomonas is round in its juvenile stage, but later assumes a pear like shape, owing to its adaptation to the tissue texture. The flagellae appear at its tapered end. If not subjected to pressure the organism appears globular in shape Propagation takes place by globular fission. However budding has been observed. The periodic disappearance of flagellatae during resting phases seems to indicate that trichomonas undergoes cyclic phases of evolution. Probably it passes through an encysted stage

The *diagnosis* of trichomonas urethritis in the male is based on the

constant presence of flagellatae in smears taken at various intervals. The characteristic aspect of the discharge, resembling watery milk, may support the diagnosis. If possible, both sexual partners should be examined. Dark field examination will easily reveal the presence of flagellatae. It must be kept in mind that, temporarily flagellatae may be absent or scarce. For this reason, repeated examination is indicated. It should also be taken into consideration that occasionally the female partner may be a carrier of trichomonas even though she presents no clinical symptoms

Therapy: There are differences of opinion concerning the therapy of trichomonas urethritis There are authors who still consider trichomonas an incidental saprophyte of the male urethra, and who consider its presence no indication for treatment, believing that it will disappear without therapy Practically however the very prolonged course and the inconvenience of the discharge demand medical attention

Unfortunately there is no specific *therapy* for trichomonas infection In trichomonas urethritis of the male every applicable bactericidal solution including protargol solution silver nitrate, and potassium permanganate solution, has been tried, most frequently with unsatisfactory results. Furthermore, none of these solutions will reach the prostate in cases in which this organ is involved Treatment by hyperthermia yields only transient remissions, although in laboratory experiments the trichomonas vaginalis is killed by temperatures of 48° to 49° C.

The results of treatment with penicillin and sulfonamides have been disappointing. Reports on the administration of other antibiotics have been too few to permit any definite evaluation of their effects It is significant that in order to obtain pure cultures of trichomonas vaginalis, penicillin must be added to the medium. Thus 250 units per cc. of medium will be sufficient to eliminate the growth of associated bacteria, leaving the trichomonas to propagate without restraint. In all cases treatment must be followed by careful surveillance over a period of months.

The role of trichomonas vaginalis in the pathogenesis of genital catarrhs in the female is thoroughly discussed in gynecological textbooks.

E. Urethritis Mycotica

Fungi have occasionally been found thriving on the urethral mucosa, and have been interpreted either as saprophytic invaders, or as secondary pathogenic elements in previously existing chronic urethritis. Damaged epithelial cells furnish a good soil for mycotic growth. The sugar content in the urine of diabetics provides another predisposing factor Occasionally the phimotic sac of the prepuce may harbor molds or fungi intermingled with numerous other micro-organisms. Fungi may also be introduced artificially during unclean catheterization The principal question,

however as to whether there exists a specific urethritis mycotica, is still a matter of discussion.

The purulent discharge produced by fungi usually shows characteristic yellow brownish or greenish color. Mycelia and spores are easily detectable in dark field examination and are rarely stained in smears. The urine is moderately turbid, with heavy threads.

Various species of fungi have been isolated from the urethra, including candida albicans, monilia, aspergillus saccharomyces, etc. Pierangeli demonstrated a primary mycotic urethritis in which the organism had most probably been transmitted from oral moniliasis (thrush) in an infant. In rare instances, mycotic plaques have been observed urethroscopically in the posterior urethra, close to the colliculus seminalis without involvement of the anterior urethra (Hell). In this case, mycelia were found in the smears and were identified by culture. The same fungi were demonstrated in specimens of smegma from phimotic prepuce.

Diagnosis

Repeated findings of mycelia and spores in the urethral discharge and in the threads of the urine are an indication for urethroscopic examination. Urethroscopy will reveal the mycotic fur spread over areas of the mucosa as whitish spots or slightly elevated, partly floating membranes. The usually striking color of the brownish, greenish or dirty grayish discharge may be the first symptom to attract special attention. However the mere presence in the smears of mycotic elements should not be lightly interpreted as a symptom of primary urethritis mycotica. As a rule, this diagnosis can be made only with reservations.

Therapy

Fungi disappear promptly following local application of a cotton swab with one to two per cent silver nitrate solution under guidance of the urethroscope. Subsequent irrigations with 3 per cent boric acid solution or potassium permanganate solution (0.1 to 500.0) will suffice to obtain a complete cure. In cases associated with diabetes, general anti-diabetic treatment is imperative for prevention of relapses.

F. Urethritis in Relation to General Diseases

- Urethritis as a Symptom in Skin Diseases
  - Urethritis herpetica
- Urethritis in Acute Infectious Diseases
- Reiter Syndrome
- Urethritis in Chronic Infectious Diseases
  - Urethritis Tuberculosa
  - Urethritis Leprosa
  - Urethritis Due to Syphilomas of the Urethral Wall
  - Urethritis as a Late Manifestation of Bilharziasis

Urethritis as a Symptom of Skin Diseases

Similar to the oral mucous membrane so also the urethral mucosa may be involved in skin rashes and dermatoses, such as allergic eruptions, erythema exudativum drug exanthemas lichen planus pemphigus etc. However reports of such an association have been rare and apparently this occasional location of these affections has not received adequate attention

Certain classical descriptions from the earlier literature should not be committed to oblivion Urban, for instance, described involvement of the urethral mucosa in a case of generalized *erythema exudativum multi forme* Flat lentil sized vesicular elevations were seen urethroscopically in the foremost portion of the urethra. Also Holzschuh described erythema exudativum of the vaginal and cervical mucosa. A mucopurulent urethral discharge has been observed in cases of *pemphigus vulgaris* due to bullous eruptions and erosions of the mucosa. In rare instances, a slight discharge has been seen in connection with *lichen planus* of the urethral mucosa. Urethroscopically the nodular efflorescences present the typical round or polygonal shape, as well as the porcelain white color characteristic of lichen planus mucosae oris In similar cases, the urethral involvement was associated with lichen planus of the larynx, or of the anal mucosa.

There are not many reports in the literature on the involvement of the urethra in *drug eruptions* In most of the instances described, the foremost part of the mucosa was the site of reactions They occurred in patients sensitive to antipyrin, cantharides, turpentine and other compounds, causing a slight discharge On urethroscopy edema, reddening or erosions were demonstrable Recently H. Haber saw a fixed" drug enanthema of the urethral mucosa in a patient sensitive to phenolphthalein (see Chapter 7 p 79)

Urethritis Herpetica. Generally speaking, the described urethral mani *festations of skin diseases are too rare to enlist the special attention of the* general practitioner This is not true, however with regard to the much more common phenomenon of *herpetic urethritis* Herpes genitalis may involve the urethra in conjunction with eruptions on the glans penis or the prepuce On the other hand, isolated herpes of the urethra is not as rare as might be concluded from the literature

The affection is always associated with discharge. Usually the secretion is scanty of a watery mucous consistency and contains some epithelial cells and leucocytes, with or without uncharacteristic bacteria. A burning sensation during micturition is the rule. The urine is clear sometimes containing a few fine threads Easily misinterpreted the sudden onset of discharge may lead to local treatment which frequently results in additional irritation thus only adding to the confusion. Slight swelling

and tenderness of the inguinal glands may precede or accompany the herpetic eruption Occasionally a doughy swelling of the dorsal lymph cord has been noted.

Some cases of herpes urethrae run a more serious course due to re lapses. The tendency of genital herpes to recur is characteristic also of urethral herpes, and thus, may offer a diagnostic clue. Urethroscopy readily reveals the polycyclic erosions, their fibrinous coating, and the surrounding fresh red areola left by the rapidly bursting herpes vesicles. The efflorescences are located predominantly in the foremost portion of the urethra.

Today the *virus etiology* of herpes simplex, i.e., of herpes febrilis as well as herpes genitalis, is established. The role of genital infection in the etiology of herpes genitalis has long been recognized. (This has been discussed in Chapter 4.) The occasional appearance of genital herpes as a prodromal phenomenon or as a syndrome in chancre or syphilitic infec tions has been emphasized in all textbooks of venereology

THERAPY Once the herpetic origin of the urethritis has been deter mined, no local treatment is indicated. The discharge disappears spon taneously with the herpetic eruptions.

Urethritis in Acute Infectious Diseases

The occasional involvement of the mucosa urethrae in *measles* has been described by Konigstein In some such cases, he observed a slight discharge lasting for several days. Jadassohn observed urethritis of probably hematogenic origin in connection with *staphylococcic pyemia*. Spence saw a mucopurulent urethral discharge in a boy of eleven years, whose father was just recovering from *mumps*. About ten days after onset of the discharge the boy was stricken with a swelling of the left parotid gland and fever During the febrile period, the discharge diminished. However soon afterwards he developed a serious orchitis, with hyperpyrexia and delirium. He made a complete recovery

No conclusive observations are available concerning the possible development of a specific bacillary urethritis in *typhoid fever* Epididymitis and prostatitis have been reported in causal connection with excretion of Eberth bacilli in the urine. Usually in these cases, no urethral discharge was demonstrable. Saphier however described one case of urethritis with findings of typhoid bacilli associated with an epididymitis during the acute stage of typhoid fever and another case of urethritis *alone* in which typhoid bacilli were identified by culture from the purulent discharge.

The problem of *amebic urethritis* has been previously discussed.

Reiter s Syndrome

In 1916 Reiter described a *triad of symptoms* which he interpreted as cardinal symptoms of a particular basic disease These symptoms

included (1) a *nonspecific urethritis* with purulent discharge; (2) a *mucopurulent conjunctivitis* and (3) *arthritis*, usually of polyarticular character

Apparently this condition is rather rare With a few exceptions, all available reports have referred to male patients, predominantly young men, of twenty to twenty four years of age Florman and Goldstein described Arthritis-Conjunctivitis Urethritis in a four year old boy

Clinical courses: In the majority of cases the full development of Reiter s syndrome is attained after two to four weeks. Frequently the *arthritic symptoms* appear later than the conjunctivitis and urethritis, and often at a time when the inflammatory symptoms of the mucous membranes had already subsided. Usually two weeks after onset of the discharge, polyarthritis develops varying in severity and course but always associated with a fever of 100° to 101 F for about ten days As a rule, the initial chill, so characteristic of the onset of rheumatic fever is lacking in Reiter s arthritic syndrome In many instances, the arthritis first tends to settle in one or two joints which remain inflamed, swollen and stiffened for several months This arthritic condition may extend over a period of four months, or as a result of relapses, up to six months. Loss of body weight and secondary muscle atrophy are marked, and may develop fairly rapidly Recovery is generally complete, however and the muscular atrophy disappears rapidly

The purulent *urethral discharge* develops rapidly sometimes as an initial symptom and in other cases after the onset of conjunctivitis. Dysuria or terminal hematuria may develop The urethritis clears spontaneously after a few weeks.

The *conjunctival syndrome* is usually mild. However in rare instances, a more severe conjunctivitis may be complicated by keratitis or occasionally by iritis.

Generally the reactions of the mucous membranes disappear not later than after two to four weeks Lasting lesions of the joints almost never remain as sequelae of Reiter s disease. However *roentgenograms* taken during the active phase of the condition, have revealed significant changes in the articular tissues resembling those observed in rheumatic fever Circumscribed areas of decalcification were seen in the subchondral areas sometimes associated with periosteal hypertrophy Roentgenograms taken during the third month of illness, showed marked osteoporosis of the approximated ends of the bones

Accessory symptoms may modify the clinical picture of Reiter s disease. Superficial lesions of the *glans penis* similar to those noted in balanitis circinata, have been reported The penis affection tends to relapse independently of the urethral condition. In other instances circumscribed

keratoderma may develop especially on the skin of the legs and the soles of the feet (Harkness) The cutaneous lesions usually clear up within two months.

Any clinical description of Reiter's disease would be incomplete without reference to the incidence of *atypical* cases, presenting only two of the three cardinal symptoms. In some cases, the conjunctivitis is lacking. Hollander reported that in one of his patients only urethral and arthritic symptoms were present. However during a relapse of the arthritis, in a later stage, conjunctivitis appeared.

Etiology: There is little doubt, that Reiter's syndrome is of infectious origin. The infectious agent remains unknown, however Various microorganisms have been suspected, as for instance, staphylococci, enterococci or more recently bacteria of the pleuropneumonia group (Dienes Ropes, *et al* 1948) Other writers believe the disease to be a virus infection. Reiter's *initial definition of the condition as a specific spirochetal infection has* not been proved. Nothing is known regarding the route of infection. There is no reason for considering this disease to be a venereal infection.

Differential diagnosis: The symptomatology of Reiter's syndrome presents many similarities to that of other diseases It is thus easily understood why *quite a few investigators feel, that evidence available at the* present time in no way justifies the generally accepted view that Reiter's syndrome constitutes a separate disease. Objections may be raised against the assumption of other authors that all these cases represent only modifications of rheumatic fever

Both arthritis and conjunctivitis also occur as complications of gonorrhea, therefore the differentiation from gonococcal infection is imperative in every case of Reiter's syndrome. Gonococci are never found in the urethral discharge in Reiter's disease. In many cases, no venereal exposure preceded the onset of the syndrome The onset of both gonococcal arthritis and rheumatic fever is usually accompanied by a chill. In Reiter's arthritis, the initial chill is absent. The failure of sulfonamide and penicillin therapy in Reiter's disease is another differential item.

Therapy: There exists no specific or otherwise noticeable effective treatment for Reiter's disease. As mentioned above the spectacular effects of sulfonamides and penicillin observed in gonorrhea, have never been seen in Reiter's syndrome The beneficial effect of aureomycin treatment in one *instance of Reiter's disease* noted by Korb and Brown (1950) may suggest further clinical trials. Evaluation of therapeutic results in such a self limited disease will always be difficult.

Salicylates are of symptomatic, not of specific value Immobilization of the involved joints offers relief during the acute stage of the disease. Diathermy may be helpful in the later stages of arthritis. Foreign protein

shock, and, in particular that following intravenous administration of typhoid vaccine seems to have some beneficial effect during the acute stage of conjunctivitis and arthritis. The urethritis, as well as the conjunctivitis, usually disappear with or without treatment, after two or three weeks.

Urethritis in Chronic Infectious Diseases

Urethritis tuberculosa: Urethritis tuberculosa usually appears as a late manifestation of advanced tuberculosis of the urinary tract. The continual exposure of the urethral mucosa to tubercle bacilli excreted in the urine favors the development of tuberculous lesions Usually the morbid process extending from lesions of the bladder and para prostatica, invades the anterior urethra, causing inflammatory infiltration with single or grouped tubercles

The tendency to ulceration soon produces an extremely painful condition. Circumscribed ulcers of characteristic appearance will develop In advanced cases, the greater part of the mucosa may be covered with florid granulations and fresh ulcers which bleed easily Periurethral nodules or cord like infiltrations may be formed. Due to caseation abscesses develop which may open either into the urethra, or externally The lesions of the urethral wall finally cause strictures which obstruct the urinary flow In the terminal stages of urogenital tuberculosis, the urethral orifice may be transformed into a gaping, bleeding ulcer making every catheterization an ordeal.

From the beginning, tuberculous urethritis is associated with seropurulent or purulent discharge containing pus cells epithelial element necrotic tissue particles and red blood corpuscles. The urine is turbid, with heavy threads and shreds. Tubercle bacilli are demonstrable in the discharge in the threads and especially the sediment of the centrifugated urine. Due to the involvement of the upper urinary tract, casts and renal epithelial cells may also appear in the urine.

As a rule urethritis tuberculosa is a *secondary* manifestation of urogenital tuberculosis The etiological diagnosis suggests itself *Primary* tuberculosis of the urethral mucosa is extremely rare Primary infection of the urethra has been reported in connection with ritual circumcision when a phthisical circumciser tried to stop bleeding by sucking the wound (*Circumcisional Tuberculosis* Schwarzwald see p 151)

Treatment In addition to the general treatment of the disease local instillations of 6 per cent guaiacol oil, or of 3 to 5 per cent iodoform oil may favorably affect the urethral lesions and will at least ease the burning pain on micturition Streptomycin, now used as a supportive measure for the general treatment of tuberculosis of the urinary tract, might be ex

pected to inhibit or arrest the tuberculous process in the urethral mucosa. However reports are not as yet advisable for definite evaluation.

Urethritis leprosa: A urethral discharge caused by the Hansen bacillus is very rare but its occasional incidence may easily lead to erroneous diagnosis. Von Bassewitz (Porto Allegre) found urethritis leprosa in a man of Caucasian origin. In this case, the skin manifestations had been mistaken and treated for syphilis. The mucopurulent discharge and a pea sized nodule palpable in the middle of the urethra were believed to be of gonorrheal origin. Since the cutaneous symptoms did not respond to anti syphilitics, potassium iodide was administered and produced an explosive reaction, with monstrous swelling of the face and of other eruptions on the skin The urethral discharge increased rapidly This reaction indicated leprosy Numerous Hansen-bacilli were found in the urethral and con comitant nasal discharge In a recent case reported by F C. Duenos and A. Ibara, *failure of penicillin therapy suggested urethritis leprosa in* a leper with concurrent gonorrhea.

Urethritis due to syphilomas of the urethral wall: The urethra is rarely involved in syphilitic processes although urethritis has been reported in initial as well as in later stages of syphilis. A primary sclerosis situated around the urethral orifice and involving the adjacent mucosa, is not uncommon. Syphilitic induration of the urethral wall, and, in par ticular of the deeper portion of the urethra, may escape notice owing to the absence of pain. It may remain undetected until induration of the regional lymph glands suggests the presence of syphilitic infection. Early routine urethroscopy in nonspecific urethritis, occasionally revealed a well circumscribed, whitish, slightly elevated lesion of the edematous mucosa as an initial symptom of syphilis.

The development of endourethral syphiloma may or may not be accompanied by a discharge. As a rule, the secretion is scanty of mucous consistency and containing only a few leucocytes and bacteria. It has a tendency to dry and may form a crust overnight sealing the urethral orifice T pallidae may be demonstrated in the discharge by a dark field ex amination. Occasionally the discharge may contain blood. Specific therapy will of course, evoke a prompt response.

Exceptionally also *chancroid* of the urethral mucosa produces urethritis. In addition to the mucosal involvement in chancroid of the urethral meatus, there are cases without any associated ulcer of the skin of the glans or prepuce although Ducrey bacilli have been demonstrated in stained smears from the purulent or sanguinolent discharge Urethroscopically the urethral ulcers exhibit all the characteristics of soft chancre, and are ex tremely painful to touch. Today local therapy is of secondary importance, owing to the striking effects obtained in chancroid with sulfonamides and

especially with streptomycin (1 gm of streptomycin daily for about five days)

Urethritis as a late manifestation of Bilharziasis: During World War II members of the Armed Forces were exposed to bilharzia infection in foreign countries. Although clinically cured by tartar-emetic treatment, many of these men developed late manifestations. Such sequelae may occur many years after apparent cure and may puzzle the physicians in this country where the disease is so uncommon.

Among the late symptoms of bilharzia infection, bilharziasis of the bladder and of the other portions of the urinary tract rank first. Sayegh, in a review of six hundred fifty three cases of late complications of this disease observed in an American hospital in Egypt, found the bladder involved in four hundred sixty two cases and the urethra in one hundred twenty seven cases. He emphasizes the fact that although the bladder is the organ most frequently attacked, it should be kept in mind that in some cases, the only demonstrable lesion may appear in the ureter or urethra, without any lesion in the bladder

The deposition of the ova beneath the urethral mucosa produces an excessive tissue reaction Some of the ova will be excreted into the lumen of the urethra, but the majority will remain in the submucosa, surrounded by leucocytic infiltration and subsequently becoming encapsulated in hypertrophic fibrous tissue Thus, large areas of the urethra may undergo fibrotic changes followed by scar formation Strictures may develop When deposited in the deeper layers of the submucosa, the ova may give rise to abscesses and to the formation of urinary fistulae especially in the perineal region Other ova remain imbedded in the fibrous tissue. Fibrosis and calcification are pathogenic of bilharziasis. Calcification is clearly demonstrable in the roentgenograms. In untreated cases intraurethral papillomas may be formed, identical with those characteristics of bilharziasis of the bladder

Corresponding to the extent of the lesions varying amounts of discharge are seen associated with dysuria and with terminal hematuria. Ova will be found in the discharge as well as in the urinary sediment. Finally damage to the kidneys results due to the formation of urethral strictures and secondary bacterial infection.

Treatment Besides the general therapy with tartar emetic directed against the basic infestation urethral bilharziasis will also require surgical treatment. Urethral strictures not responding to dilatation with graduated sounds must be operated upon Surgical treatment is indicated also for the extirpation of fistulas and papillomatous proliferations should be destroyed by fulguration.

G Urethritis Associated with Neoplasms of the Urethral Wall

Urethritis Due to Intraurethral Condylomata Acuminata
Urethral Caruncles of the Female
Urethritis Due to Malignant Neoplasms

Urethritis Due to Intraurethral Condylomata Acuminata

Intraurethral warty excrescences of the anterior urethra occur in association with *condylomata acuminata* of the external genitals. In the vicinity of the orifice they propagate exuberantly. Urethroscopy will often reveal the presence of additional excrescences in other parts of the urethra. On the other hand, the urethra may be the only location. Solitary intraurethral warts occur in both sexes. In the majority of cases, these intraurethral proliferations are part of a general eruption of condylomas distributed over the glans and coronary sulcus of the penis, or over the mucosa of the vaginal introitus. In propagating, they may impede the urinary outflow. Intraurethral condylomata acuminata appear urethroscopically either as pediculated or flat excrescences of a pink to dark red color.

In the male, the fossa navicularis and the anterior third of the urethra are the sites of predilection. Condylomata acuminata are encountered less frequently in the posterior urethra and rarely on the mucosa of the colliculus seminalis. In this location, they usually appear as flat, multiform polypoid elevations.

Histologically these proliferations of the anterior urethra are identical with condylomata acuminata. They are benign acanthomas. Condylomata acuminata of the posterior urethra may differ clinically from those of the anterior portion, resembling more nearly the type found in papillomatosis of the bladder.

The presence of a few intraurethral condylomata acuminata suffices to cause chronic urethritis with more or less mucopurulent discharge. Due to the vulnerability of all urethral papillomas, bleeding may occur spontaneously or as hematuria after micturition, or following introduction of instruments. Introduction of the urethroscope or even a slight touch with a cotton swab suffice to cause hemorrhage. Papillomas of the colliculus seminalis often produce annoying nocturnal erections. In the female, single condylomata acuminata of the meatus occasionally appear as everted bulges of the mucosa. Protruding from the meatus they may be mistaken for urethral caruncles. The latter, however, differ essentially from condyloma acuminata. Frequently the development of caruncles is preceded by or associated with urethritis.

Treatment. Urethritis disappears promptly following removal of the excrescences. The topical application of podophyllin to condyloma acumi

nata, as now widely used, would hardly be suitable for intraurethral application especially in the deeper parts of the urethra. In both sexes, papillomas of the urethra can be easily removed surgically or by fulguration under the guidance of the urethroscope. Papillomata of the posterior urethra in the male should be subjected to histological examination, followed by a general check up of the urinary tract.

Urethral caruncles: There are different varieties of caruncles the type under discussion presenting the features of a chronically inflamed proliferation. Histologically there is edema, vascular engorgement and a more or less intense inflammatory infiltration, sometimes associated with nodular accumulation of lymphadenoid tissue elements (Lipschütz)

Urethral caruncles of the female cause also stabbing, shooting or burning pains and occasionally slight bleeding at the beginning or the end of micturition following intercourse, friction or trauma In addition dysuria urgency and increased frequency of urination may be noted. F B Block, in his elaborate study on the female urethra, described the gross appearance of caruncles in the female as a "bright red growth like a miniature cock-comb or like a very small raspberry springing from the lower margin of the meatus urethrae. Its size may vary from that of a pin head to that of a pea. *Caruncles occur as single or as multiple strictures*

Urethral caruncles are benign in character However Ratner and Schneidermann described an unsuspected early squamous cell carcinoma, discovered incidentally in the examination of an excised urethral caruncle. These authors are inclined to look upon urethral caruncles as precancerous lesions and recommend radical removal of every caruncle with the electric bistouri or loop followed by fulguration of the base

Urethritis Due to Malignant Neoplasms

As a rule malignancy of the urethral wall is accompanied by secondary urethritis. Discharge may be the initial clinical manifestation of a primary *tumor of the urethra. Inconspicuous at first, the serous or mucous secretion* may escape attention for a time and thus preclude an early diagnosis.

Primary urethral carcinoma is not extremely rare Recent statistics seem to indicate that females are more frequently afflicted. Usually the tumor develops after the menopause In the male primary carcinoma of the urethra is rarely encountered before the age of forty five years and persons of advanced age seem to be most susceptible In very rare instances, urethral carcinoma has been reported in individuals from eighteen to twenty five years of age

In the *female* this tumor formation presents itself as a more or less hard, fixed neoplasm of the urethral meatus occasionally involving the adjacent vaginal mucosa. Frequency and difficulty of micturition are

common clinical symptoms. In the *male* carcinoma urethrae has been found predominantly in the pars bulbocavernos which is the site of predilection for urethral stricture. Cicatrization in any part of the wall of the urethra may constitute a precancerous lesion

The extent and rate of tumor growth will determine the clinical picture of urethral carcinoma. The discharge may become purulent and may contain blood and uncharacteristic bacteria. Invasion of the periurethral tissue by tumor cells will produce diffuse infiltrations of the penile tissues with occasional fistulization. Extension into the perineal tissue involvement of the lymph glands and metastases complicate the later stages of the disease.

Basal cell carcinoma is the most common form encountered, whereas cylinder cell carcinoma is unusual and adenocarcinoma is extremely rare. Generally primary carcinoma of the female urethra offers poorer chances for successful radical surgical removal than carcinoma of the male urethra. In a review published by Seng and Siminowich, only one of six women operated upon for primary urethral cancer was alive after five years.

Diagnosis: An early diagnosis is particularly difficult in carcinoma of the male urethra. Every nonspecific urethritis which cannot be otherwise explained should be subjected to urethroscopy Suspicious changes in the intraurethral picture may offer a diagnostic clue even before palpation indicates the presence of a neoplasm.

Therapy: The treatment is surgical and should be combined with postoperative Roentgen irradiation Technical details are found in surgical manuals.

H Urethritis Due to Mechanical, Thermal or Chemical Lesions of the Urethral Mucosa

Urethritis Traumatica. Urethritis Due to Intermittent Prolonged Traumatization
Urethritis Associated With Excretion of Corpuscular Constituents in the Urine
Urethritis Due to the Introduction of Foreign Bodies Into the Urethra
Urethritis and Catheterization
Thermal Urethritis
Chemical Urethritis
Urethritis Possibly Caused by Excretion of Irritating Substances Dissolved in the Urine
Congenital Urethritis
Urethritis Associated With Itching Dermatoses of the Genital Region (Reflex Urethritis)

Although of most varied origin urethritic conditions due to mechanical injury of the urethra, present certain characteristics of diagnostic significance These characteristics are (1) sudden onset without any apparent incubation period (2) rapid development of symptoms, quickly arriving at their climax, (3) inflammation often associated with edematous

swelling (4) difficulties in micturition (5) pains (6) serous mucous or mucopurulent discharge with or without admixture of blood, and (7) spontaneous recovery following elimination of the irritating cause Prolonged irritation results in chronic urethritis. Secondary bacterial urethritis demands special antibacterial therapy

Urethritis Traumatica

Urethritis due to traumatization Urethritis attendant upon trauma of the lower urinary tract often persists long after the primary lesion has healed. Cicatrization of wounds caused by missiles or by accidental rupture of the urethra gives rise to the formation of strictures and occasionally of diverticula, or urethral fistulae—thus preparing the ground for the development of a secondary bacterial urethritis This discharge is usually purulent and may be mixed with blood. Microscopically a great variety of bacteria will be found.

Diagnosis: Retrograde urethrography and cystography with a radio-opaque contrast medium are indispensable for detection and location of all the lesions involved in cases of severe trauma.

Treatment: Urethritis associated with slight trauma of the urethra, will disappear spontaneously when the primary lesion is cured. In more serious cases the posttraumatic urethritis will not clear up completely before strictures, diverticulae and fistulae have been surgically removed. A local treatment may yield transitory relief in cases with inconspicuous residual scars without traumatic strictures. Even small circumscribed changes in the urethral wall may be the cause of relapses of secondary urethritis after trauma. Periodic control, including urethroscopy will be helpful in ascertaining the cause of relapses in posttraumatic bacterial urethritis.

Urethritis Due to Intermittent Prolonged Traumatization

In his office the practitioner may be confronted with a mild form of nonspecific urethritis caused by a prolonged exposure of the perineal region to repeated and continuous concussion We have not infrequently had the opportunity of observing this condition in chauffeurs and motorcyclists, who without any preceding sexual exposure came to the office for a clear diagnosis and treatment of a serous or mucous secretion appearing before voiding the morning urine Usually the discharge was scanty occasionally drying overnight to form a crust sealing the urethral orifice. Diagnostically one must also bear in mind that this type of traumatization can likewise lead to prostatorrhea or spermatorrhea which must not be mistaken for an urethral discharge

Urethritis Associated With Excretion of Corpuscular Constituents in the Urine

Any excess in the *excretion of urinary salts* can lead to the development of an urethral discharge. Minute particles of phosphate, urate or oxalate crystals, passing continuously through the urethra will finally produce an inflammatory irritation. The freshly voided urine is hazy or turbid. Large quantities of crystals are seen in the urinary sediment and are easily identified by chemical tests.

The discharge varies in amount corresponding to that of the salt excretion. The secretion is usually mucous, and sometimes contains traces of blood. Microscopically some epithelial cells and a few leucocytes are present Bacteria are lacking or scanty and uncharacteristic. Urethritis due to phosphaturia and similar conditions should not be subjected to local treatment owing to the risk, thus incurred, of still further increasing the chemical irritation. Internal therapy of the general condition responsible for the excessive salt secretion is the only way to cure the secondary urethritis.

This mild form of urethritis presents a sharp contrast to the serious condition resulting from the deposition of single or multiple large urinary concrements in the urethra. As soon as the calculus exceeds the calibre of the urethral lumen it may remain incarcerated for a long time, acting as a foreign body and causing edema, pains, purulent discharge and occasionally bleeding. Finally increasing urgency and dribbling micturition every fifteen to twenty minutes produces a state of emergency which imperatively demands surgical intervention.

As a rule the calculus enters the urethra from the bladder However the formation of concrements *in loco* is not uncommon in congenital diverticula, or in diverticula associated with old urethral strictures. In rare instances, even large concrements located in urethral diverticula may be carried for a long time without great inconvenience Neugebauer and in a similar case, Nobre described diverticula stones of giant proportions (weighing 89 and 170 gm. respectively) being tolerated for a long time.

Endourethral calculi occur most frequently in males. The *female* urethra is short and larger in calibre than that of the male. For this reason, vesical calculi pass more easily through the female urethra. Primary calculi due to congenital or acquired dilatations of the urethral wall of the female are extremely rare

Diagnosis: Urethritis associated with large intraurethral calculi, presents little diagnostic difficulty In addition to dysuria, pains, and inhibition of the urinary flow there appears a characteristic, circumscribed swelling of the urethral wall indicating the presence of an incarcerated

foreign body The calculus can usually be palpated from the perineum However smaller calculi may remain undetected when this swelling is absent and the burning sensation on micturition may be attributed to the presence of a nonspecific urethritis. The importance of Roentgen diagnosis in every case suspected of intraurethral concrement, is evident.

The diagnosis of a diverticulum without corpuscular contents is easily accomplished by palpation of the urethral wall. A mass can be felt on the inferior side of the urethral wall and empties on pressure with escape of discharge from the meatus. The discharge is milky or purulent The urine is turbid. Diverticulae are easily demonstrable by urethrography or roentgenography

Urethritis Due to the Introduction of Foreign Bodies Into the Urethra

Urethritis and catheterization: Foreign bodies introduced into the urethra intentionally or by accident will cause acute and chronic urethritis The slightest injury to the mucosa will serve as a portal of entry for bacterial invasion. The symptoms produced vary with the shape, size and consistency of the object introduced.

Parts of broken catheters or of defective bougies may enter the bladder or remain in the anterior urethra Such accidents occur usually in prostatics during the course of prolonged self-catheterization. However even the use of improperly cleaned instruments or of instruments worn rough by long usage, or the prolonged use of irritating lubricants and disinfectants may suffice to produce urethritis and subsequent involvement of the bladder Even when performed in conformity with all the rules of medical art, catheterization may occasionally produce urethritis. Chronic urethritis is almost inevitable as a result of indwelling catheters The urethritis may also persist and require treatment long after catheterization has been discontinued. The therapy is the same as that for nonspecific urethritis

Judging from the literature, the variety of *deliberately* introduced foreign bodies is truly grotesque. Such objects or parts of them usually introduced by children or by psychopathic adults remain in the urethra and their presence may be kept a secret by the individual for weeks and months Eventually edema, discharge and difficulties in micturition wring a confession from the culprit. Straws grain stalks wood particles, glass tubes hairpins and nails have been visualized in roentgenograms. Pointed splinters of straw or awns of grain piercing the urethral mucosa may easily escape detection As they very shortly become buried in the swollen mucosa, such objects may be responsible for prolonging a purulent discharge for months.

Urethritis of such origin will not respond to any treatment until

the foreign body has been removed, frequently a difficult urologic or surgical problem. Serious complications may follow the incarceration of such foreign bodies. Szpèr reported total gangrene of the penis due to an incarcerated piece of charcoal, imbedded in an urethral diverticulum. In this case surgical removal of the object could no longer prevent the fatal issue

Urethritis due to the excretion of *animal foreign bodies* in the discharge or urine has been described as a clinical curiosity Cases have been reported in which nematodes larvae of flies and other insects, were found in patients with or exceptionally without a pre-existing urethritis. The route of infestation of animal parasites gaining entrance to the urethra has remained obscure in nearly all cases reported.

Fischer found the larvae of a fly species in the discharge and urine of a patient with post gonorrheal catarrh. Sprehn found the nematode diplogaster lirata in one case of acute nonspecific urethritis

Sternberg was able to explain the entrance of larvae of niptus hololeucus into a patient with post-gonorrheal urethritis. The beetle in question had deposited some eggs near the opening of the syringe used for injections. The eggs were then injected with astringent solution. This mode of infestation was also confirmed experimentally Sternberg exposed several syringes to beetles found in the patient's stone house and succeeded in obtaining a deposit of eggs on one of the syringes. These eggs were then injected into a healthy man, who then complained of irritation in the urethra on the tenth day after the injection Shortly thereafter he developed a discharge in which a larva was found.

Thermal urethritis: Thermal urethritis is uncommon. It may be caused inadvertently by the introduction of insufficiently cooled metal instruments, or by incorrect application of diathermy The diathermy treatment of urethritis with bougie electrodes as employed in some countries in the nineteen-twenties has now been abandoned. However the use of diathermy in the treatment of rheumatic pains in the loins or small of the back, may also lead to urethritis if the electrodes have been improperly placed. Joseph reported one such case following diathermy treatment for lumbago. One electrode had been placed over the loin and the other over the symphysis. After the fifth treatment, a urethral discharge appeared which could not be explained otherwise The discharge was serous, containing some epithelial cells and leucocytes. No bacteria were found. The discharge subsided when diathermy treatment was discontinued.

Chemical urethritis: In this age of sulfonamide and penicillin or aureomycin therapy of gonorrhea and of other forms of urethritis, chemical urethritis has become a condition of minor importance. Formerly irritation of the urethral mucosa was often caused by the injection of strong

anti-gonococcal and antiseptic solutions, the continued use of which might produce a discharge persisting over a long period. In such cases, the patient, as well as the physician were easily misled to believe that the gonorrhea had not been cured. In order to make sure, still stronger solutions were then used, only to delay the healing process. Cessation of treatment at *intervals finally permitted a realization of the actual* conditions.

Our Public Health Organizations have made an effort to reduce the incidence of another form of chemical urethritis, namely the type known as *"urethritis a prophylaxi."* The selection of local prophylactics cannot be left to the patient's undirected choice. Single or repeated injections immediately following sexual intercourse for the purpose of preventing infection may result in urethral catarrh. The prolonged use of strong prophylactic agents will readily produce symptoms exactly like those of the disease the patient is trying to escape. Upon cessation of these injections his mistake soon becomes evident.

In a like manner urethritis may follow the use of *contraceptive drugs* The transitory character of the irritation makes the diagnosis self-evident.

During World Wars I and II, a special form of chemical urethritis claimed the attention of physicians in the Armies of all involved nations. *Self inflicted urethritis* was used by shirkers to simulate venereal disease. Soldiers weary of war or psychopathic individuals resorted to this device in order to be hospitalized. The methods and agents employed were perplexing Solutions of ammonium chloride pyroligneous acid, benzine, mercury bichloride silver nitrate etc. were injected, resulting in a purulent and sanguinolent discharge, not infrequently associated with edema of the penis and in more severe cases, followed by gangrene In the majority of cases recovery was slow Secondary bacterial infection produced complications of the upper urinary tract and following the prolonged use of caustic solutions strictures were not infrequently formed.

Similar lesions of the urethral mucosa, occasionally accompanied by bloody and purulent discharge may also be encountered after *mistakenly* employed caustic solutions during gonorrheal treatment. The arbitrary use of strong solutions played an important role in the self treatment of gonorrhea and occasionally in its treatment by quacks. Fortunately the stormy onset of chemical urethritis *with a sanguinolent discharge and violent* pains forces an interruption of such unauthorized therapy and the consultation of a physician.

Urethritis Possibly Caused by Excretion of Irritating Substances Dissolved in the Urine

Opinions differ as to whether there exists an urethritis *primarily* induced by excessive indulgence in *alcoholic* liquors Novy who made

a study of this question gave an affirmative answer He remained uncertain only as to whether the alcohol per se or the added aromatic or spicy mixtures must be held responsible for the urethritis following alcoholic excesses. The urethral discharge although generally scanty was always present even in individuals who had no previous history of gonorrhea. The discharge was mucous containing some epithelial cells and a few leucocytes, but rarely bacteria. Urethroscopically Novy found a slight to moderate hyperemia of the anterior and posterior urethra.

The correct answer to this question must await more thorough investigation, but there is no doubt that excessive indulgence in alcoholic liquors will exacerbate the discharge. This is true in both chronic and acute gonorrhea. The widely employed alcohol test of the past constituted one of the earlier provocative methods for demonstration of "latent gonococci, which could not be detected in smears from the morning drop in chronic gonorrhea. Cultural methods vaccine injections and mechanical provocation are more up to date.

Even more problematic is the assumption of a condition designated as *urethritis ab ingestis*" that is, an urethral discharge due to the habitual ingestion of strongly spiced or peppered food. This question can be answered only with reservations. It is true that the excretion of certain drugs, such as cantharides, turpentine, scilla, and iodine compounds, may cause a burning sensation during micturition and is occasionally associated with minimal amounts of discharge. Our present knowledge, however is limited to the experience of an irritating effect of a strongly spiced diet in previously existing urethritis.

Congestive Urethritis

This form of urethritis involves predominantly the posterior part of the urethra. Chronic hyperemia due to sexual excess coitus interruptus, or perversity can produce a slight urethral discharge The urine is clear and may contain some threads, consisting of mucus and some leucocytes Redness and swelling of the colliculus seminalis are demonstrable by urethroscopy The majority of these patients present the symptoms of sexual neurasthenia, prostatorrhea and spermatorrhea, associated with general nervous manifestations.

Urethritis Associated With Itching Dermatoses of the Genital Region (Reflex Urethritis)

A. Dreyer was one of the first to direct attention to the phenomenon of reflex urethritis. An urethral discharge can appear as a reaction to itching dermatoses of the genital region. Scabies of the anogenital area produces annoying pruritus and violent scratching. According to Dreyer

there is a slight or minimal discharge of a watery or mucous consistency Today this phenomenon is well known as a symptom of scabies phthiriasis, and pediculosis. Drever interpreted this form of urethritis as a result of reflex processes However the frequent coincidence of scabies infestation with venereal infection must be taken into consideration in making such a diagnosis

Formerly Bartrina reported that occasionally urethritis occurs in direct connection with incarcerated stones of the urethra or with nephrolithiasis. He found a slight to moderate discharge, associated with a burning sensation on micturition. Bartrina explained this symptom as the result of a renal-ureteral-urethral reflex. However there remains the possibility of a direct irritation of the urethral mucosa by urinary urates even if these are completely dissolved in the urine. Here, too we have a problem for further clinical investigation.

I Non-gonococcal Infection of Accessory Canals of the Urethra or of Congenital Canals and Cysts of the Genitoperineal Raphe

Infection of accessory urethral canals represents a well known complication in acute gonorrhea. Before the introduction of the sulfonamides and penicillin into the therapy of gonorrhea, this complication when undetected and untreated, furnished a frequent source of continual reinfection of the urethral mucosa. Incidences of primary isolated gonococcal infection of the accessory canals without involvement of the urethra have been observed sporadically

The accessory ducts, found dorsally and ventrally to the urethra vary *considerably in length. They may be mistaken for lacunae or small diverticulae* They form blind-ending ducts or may communicate with the urethral lumen or with the skin

Exceptionally infections of these canals caused by organisms other than gonococci, have been described. They occurred either in connection with nonspecific bacterial urethritis, or very rarely as primary infections. Most characteristic is Waelsch s observation of a pseudodiphtheritic infection in a patient with accessory canals and hypospadia. A small nodule had formed near the widely open meatus a few days following intercourse Spontaneous regression was soon followed by suppuration, perforation and fistulation, the mucopurulent secretion showing pseudodiphtheria bacilli in pure cultures microscopically as well as after cultivation The urethra was not involved.

Very rare are similar infections of congenital canals and cysts of the genitoperineal raphe which may be found anywhere along the raphe whether on the prepuce scrotum or perineum. These canals may communicate with the skin by one or several openings. Acute redness swelling and

pains are indicative of secondary infection. Circumscribed or more extensive infiltrations ensue the thin walled cysts often rupture spontaneously Staphylococci, streptococci coli bacilli or other bacteria may be found

Similar infections of accessory ducts in the female will be discussed in connection with non gonococcal disease of Bartholin s glands.

Histologically the stratified squamous epithelial lining of the infected canal or cyst is more or less destroyed and inflammatory symptoms dominate the picture.

The *differential diagnosis* may include chancroid infection, lymphogranuloma venereum and tuberculosis.

Treatment

The described infections of these congenital formations demand either surgical removal or electrothermic destruction (especially electrocoagulation) To determine the extent and course of accessory urethral canals, the introduction of a fine sound will frequently yield satisfactory results. In more complicated structures, the injection of a radio-opaque substance will be found helpful in the Roentgen demonstration of the peculiarities of the anomaly Urethrography proved of special value in one case, revealing a curved or Y-shaped course of the accessory urethral canals having both intraurethral and external terminations.

J "Nonvenereal" Stricture of the Urethra

Acquired Forms Congenital Strictures of the Urethra

Acquired Forms

The term nonvenereal stricture refers principally to *non-gonorrheal* strictures of the urethra. *It is only in exceptional cases that the rare* syphiloma of the periurethral tissue causes an obstruction of the urethral lumen. Until a few years ago gonorrhea ranked first in the etiology of urethral stricture. Statistics from the first decades of our century recorded a gonorrheal or post-gonorrheal origin in 80 to 90 per cent of all urethral strictures During the period of both World Wars the incidence of post traumatic strictures showed a marked increase whereas that of post gonorrheal strictures diminished rapidly following the dramatic rise in cures of gonorrhea due to modern sulfonamide and penicillin therapy

Traumatic strictures, as a consequence of common accidents or of injuries due to gunshots and explosive missiles represent the end-effects of cicatricial processes involving the periurethral tissues. Such scar formation is much more extensive and deeper than that following gonorrhea. The scar tissue is also more rigid and not infrequently shows ramifications extending into the penile tissues. Distortions and corkscrew-like torsions of the ure-

thra present most unfavorable conditions for instrumentation and operative procedures Diverticular pockets may develop or fistulae as a result of secondary infection Multiple strictures although occurring occasionally as a result of gonorrheal lesions are much more common following traumatic injury In some instances a stricture may develop due to perforation of the urethral wall by improperly performed or roughly enforced catheterization. Urethral strictures may also be produced by caustic lesions, caused by inadvertent injection of highly concentrated chemical solutions Special attention has been directed to the increasing incidence of postoperative stricture, following the popular transurethral resection for the relief of bladder neck obstruction. Traumatic stricture of the *female* urethra is rare as compared with that of the male urethra, and is usually a result of obstetric trauma.

The *clinical symptoms* vary according to the degree of injury Discharge *is either scanty and mucous or abundant and purulent. The urine* is more or less turbid with shreds and threads. Frequency and urgency painful micturition, dribbling, and deviations of the urinary jet complete the clinical picture Secondary infection involves the upper urinary tract.

Differential diagnosis As a rule, traumatic stricture manifests itself much earlier than post gonorrheal stricture which rarely gives clinical symptoms before a year s duration. Gonorrheal strictures are located predominantly in the bulbomembranous portion of the urethra and never involve the prostatic portion. Traumatic stricture may involve any part of the urethra.

Treatment In the majority of strictures resulting from war wounds or serious accidents surgical removal of the obstructing scar tissue becomes imperative Many strictures of traumatic origin may be impenetrable by usual methods of dilatation or introduction of sounds. Urethroscopy and retrograde urethrography with a radio-opaque contrast medium, will be required for diagnosis of the extent and localization of the scar tissue and for determining the type of operative procedure. Surgical removal of traumatic strictures must be followed by periodic control and gradual dilatation over a prolonged period of observation in order to maintain the result obtained by operation. Detailed information about diagnostic and therapeutic procedure can be found in urological textbooks.

Nonvenereal strictures may also develop in connection with chronic inflammatory diseases of non gonorrheal type, such as tuberculosis bilharziasis or lymphogranuloma venereum In advanced cases, sclerotic changes or polypoid excrescences may impair the urinary outflow Finally the presence of malignant growth may be the cause of obstruction as in advanced cases of primary or secondary cancer of the penile tissues involving the urethral wall.

Congenital Strictures of the Urethra

Congenital strictures of the urethra are not uncommon if one includes the congenital stenosis of the external meatus urethrae which occurs in both sexes, but predominantly in the male Extreme constriction may lead to serious renal damage in children owing to persistent urinary retention Ulcerative meatitis is a frequent complication. A scab forming overnight in such cases is easily wiped off with resulting bleeding After healing, the constriction may be increased by subsequent scar formation. In these cases, an early meatotomy is indicated.

Congenital stenosis located elsewhere in the urethra of children are exceptional and may respond to gradual dilatation with sounds In the female, congenital stenosis of the meatus seldom requires meatotomy and usually responds readily to periodical dilatation with sounds (Campbell)

Of most important diagnostic significance is the presence of urethral *diverticula* which may be either congenital or acquired. Congenital diverticula are most common in male subjects, whereas acquired diverticula predominate in females. The formation of diverticula is frequently associated with valve-like obstacles found near the pouch of the urethral wall. It is their presence that may lead to retrograde urinary retention with secondary bacterial infection of the urinary tract.

Differential diagnosis: Diverticula of the male urethra are characterized by a tumor like swelling at the penoscrotal or perineal region and must be differentiated from other tumor formations, such as concrement deposits which will change the consistency of the palpable swelling Otherwise the diagnosis is easily corroborated by the escape of urine on pressure and by the variation in the size of the tumor in proportion to the amount of accumulated fluid. If this perineal swelling should be lacking in an individual case, the diverticulum may remain undetected for a long time

Gross and Bill stressed the possible fatal consequences in three cases of urinary obstruction in children The cause of the obstruction was not recognized in two cases and in these the outcome was fatal The third infant recovered quickly following surgical removal of the diverticulum and its valve-like obstacles.

K. Non-gonococcal Discharge in Children

Genital discharge in children occurs predominantly in girls, and is caused most frequently by gonorrheal infection However discharges of non-gonococcal origin are not uncommon. They may be produced by bacterial infections other than gonococcal, by mechanical irritation intestinal parasites, or by constitutional factors.

Anatomically the genitals of the female infant are rather unprotected

and therefore more readily contaminated. Non-gonococcal bacterial urethritis in boys is very rare (Sherborne and Warthin acute urethral dis charge *in a six and one-half year old boy due to streptococcal infection)*

Numerous micro-organisms have been supposed to cause non-gonococcal vulvovaginitis in children Gram-negative diplococci, hemolytic streptococci, staphylococci pneumococci, diphtheroids and coli bacilli have all been considered as etiological agents In a great number of cases the specificity of the respective organisms could not be satisfactorily proved. Definitely however streptococci, pneumococci, diphtheroids and coli bacilli have proved to act as pathogenic organisms

The discharges observed in non-gonococcal genital catarrhs of children are either slight and mucous or more abundant and mucopurulent. McGinness and Telling described an incontestable case of vulvovaginitis caused by Shigella flexneri. The seven year-old girl contracted diarrhea seven days before onset of a copious purulent discharge. Diphtherial vulvovaginitis occurs in connection with diphtheria of the throat or occasionally as an isolated infection.

Vulvovaginitis in children develops frequently as a consequence of *oxyuriasis* The mucous discharge is either abacterial or contains uncharac teristic bacilli, cocci, and diplococci These catarrhs tend to recur or may run a chronic course unless the infestation by intestinal worms has been revealed. The discharge readily leads to secondary inflammation of the vulvar and perianal region associated with pruritus.

Intestinal worms other than oxyuris vermicularis rarely reach the anal and genital openings Vulvovaginitis ascribed to intestinal infestation by *ascaris lumbricoides or trichocephalus dispar may be explained by the ab*sorption of toxic products from the infested intestine.

Pediatricians have directed attention to the role of constitutional factors in the pathogenesis of vulvovaginitis infantum (anemia, malnutrition eczematous diathesis tuberculosis) Siminowich found abnormal constitu tional conditions in forty-one out of fifty children with non-gonococcal vulvovaginitis aged nine months to thirteen years. Of this series sixteen presented a "lymphatic constitution.

Differential Diagnosis

The demonstration of certain bacteria constantly present in a series of smears should always be supplemented by culture methods to rule out a gonococcal infection and to identify the respective micro-organisms. Acute discharge in boys should always suggest the possibility of a foreign body introduced into the urethra. However as emphasized by Schacht also in girls an abacterial or bacterial discharge may be provoked by for eign bodies. In order to exclude this possibility the examination should in

clude a digital rectal examination. Dellopiane, for instance, found a mussel shell in the vagina of a seven year-old girl with chronic discharge. Its presence had remained undetected for months. Stoeber found as many as thirty small foreign bodies in the vagina of a two and one-half year old girl as sources of purulent discharge.

Treatment

Cleanliness rinsing with mild disinfectant solutions and local application of dusting powders in association with internal medication will suffice to cure vulvovaginitis due to oxyuriasis. Genital discharges caused by constitutional factors subside spontaneously after cure of the basic condition.

Bacterial catarrhs often respond to rinsing and lavages with solution potassium permanganate, 1/3000 to 1/5000 In more obstinate instances, however an additional treatment with sulfonamides or antibiotics may be helpful, especially in streptococcal, pneumococcal or pseudodiphtherial vulvovaginitis. Sherborne and Warthin, in the above mentioned case of streptococcal urethritis in a boy noted prompt response to sulfadiazine (1 gr per kg. of body weight daily divided into four daily doses for a period of five days) In bacterial vulvovaginitis Schacht administered sulfadiazine either orally or in the form of suppositories containing 7½ gr (0.5 gm) each, introduced nightly for one week. McGinness and Telling obtained complete recovery by administration of sulfaguanidine in vulvovaginitis due to Shigella infection

When selecting an antibiotic compound, the failure of penicillin in non-gonococcal urethritis in adults must be considered. Aureomycin or terramycin may be effective in certain cases.

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CHAPTER 18

NONVENEREAL DISEASES OF COWPER S AND BARTHOLIN S GLANDS INFECTIONS OF SKENE S DUCTS

Cowper s Glands Bartholin Glands
Infections of Skene s Ducts

Cowper s Glands

Cowper s glands (bulbourethral glands) are pea-sized organs symmetri cally located in the trigonum urogenitale of the male and are embedded between the muscle fibers of the musc. transversus perinei. Their main ducts open into the pars bulbosa urethrae. Their secretion lubricates and alkalizes the urethral mucosa during erection and intercourse

Acute inflammatory lesions of these glands other than gonorrheal are uncommon but may develop in association with bacterial urethritis and prostatitis A painful pea to bean sized induration, usually unilateral, develops at the perineum, with a tendency to softening Pus empties spon taneously into the urethra, but never outwards through the perineal tissue.

Chronic inflammation of Cowper s glands leads to obliteration of the main ducts and to cyst like dilatations, which occasionally may harbor concrements. Laquière and Bouchard described cowpérite calculeuse with twenty to thirty small phosphate concrements in a pocket of the extremely dilated duct.

Cowperitis tuberculosa occurs as a secondary affection in urogenital tuberculosis Primary tuberculous cowperitis is a clinical curiosity (one such case was described by Papin and Vafiadis)

Carcinoma of Cowper s gland may develop secondary to urethral carcinoma. Primary carcinoma of Cowper s gland is very rare. Early diag nosis is difficult. The differentiation between cancer of Cowper s gland and urethral cancer is almost impossible in advanced cases unless postmortem findings render a final proof as to whether the neoplasm originated in Cowper s gland or in the urethral wall. Urethral carcinomas are predom inantly squamous cell carcinoma whereas the glandular pattern dominates the histological picture in carcinoma of Cowper s gland.

Primary cancer of the afflicted gland manifests itself as a nodular mass, palpable from the perineum and rectum. Discomfort may be felt, aggravated by sitting. The onset of urinary disturbances (dysuria, frequency) points at an involvement of the urethra. In ultimate stages, perforation through the perineal skin by the propagating tumor and ulceration may occur.

A doubtless primary carcinoma of Cowper's gland has been described by Griesau and Lipphard (1951). The sixty-six year old patient was admitted in complete urinary retention. He was unaware of the painless perineal mass causing his condition. Autopsy revealed an adenocarcinoma derived from Cowper's gland. A similar case with review of the literature has been reported by Uhle and Archer (1935). Treatment is surgical.

Bartholin's Glands

Bartholin's glands (vulvovaginal glands) in the female are the analogues of Cowper's glands in the male. They are located symmetrically between the sheaths of the fascia perinei, their ducts opening at the inner



FIGURE 157. Acute abscess of Bartholin's glands.

side of the labia minora, about in the middle between the urethral orifice and the posterior commissure.

Inflammatory lesions are predominantly of gonorrheal origin but occasionally are caused by other infections (coli bacilli, streptococci). In acute bartholinitis, pseudoabscesses readily develop due to obstruction of

the narrow excretory duct and the accumulation of pus. Clinically acute non-gonococcal bartholinitis produces the same egg-shaped swelling at the inner side of the labia minora as characteristic of gonococcal bartholinitis, thus causing a more or less circumscribed infiltration and subsequently a protruding tumor which may overlap the introitus.

Cyst formation is a frequent sequel of chronic bartholinitis. These cysts show periodical swellings or recession according to their accumulated



FIGURE 138. Chronic infection of Bartholin's gland with fistula. (F Callomon, Die Nichtvenerischen genitalerkrankungen. G. Thieme Leipzig, 1928, p. 155)

contents. Cysts of the Bartholin glands also occur after obstetric injury when cicatrization has obstructed the ducts. Congenital cysts of Bartholin's glands are very rare anomalies

It is a common experience that still after a definite cure of gonorrhea of the female some mucopurulent secretion may be obtained from the ducts by pressure containing a variety of bacteria other than gonococci. This form of postgonorrheal bartholinitis may persist for an undetermined time. However nongonococcal bartholinitis occurs also in patients with no history of gonorrhea.

In typhoid, acute bartholinitis has been described as a consequence of urinary excretion of typhoid bacilli and exceptionally also due to metastatic

infection of the glandular tissue. Typhoid bacilli may then be found in pus from the abscess cavity

Primary cancer of Bartholin's glands is one of the rarest neoplasms of the female genital organs. The initial lesion may remain unnoticed for a long time. In a case reported by Crossen (1948) the inconspicuous mass had been present for fifteen months before the first trip to the physician. In early stages, the solid little tumor may be freely movable over the underlying tissue. The regional lymph glands are involved rather late.

Almost without exception carcinoma of Bartholin's glands develops after the menopause. The characteristic clinical features of malignancy in these cases are (1) unilateral location deep in the posterior and lower half of the labium majus (2) distinct demarcation, and (3) a hard consistency in marked contrast to the characteristics of chronic suppurative bartholinitis. Biopsy is imperative. *Histologically* these neoplasms have their origin either in the ducts (epithelioma) or in the glandular cells (adenocarcinoma, with or without cyst formation)

The *differential diagnosis* includes lymphogranuloma venereum and malignant neoplasms, next to gonorrheal or postgonorrheal bartholinitis. Lymphogranuloma venereum may involve Bartholin's glands, especially in cases with extensive changes of the vulva. Moeller described a primary infection near the opening of Bartholin's duct as an initial symptom of lymphogranuloma venereum. The problem of foremost importance here lies in the distinction of these affections from malignant tumors.

Treatment: Pseudoabscesses in acute infectious bartholinitis demand incision and drainage. In untreated cases fistulation may result. Of decisive importance is an early recognition and surgical treatment of malignant neoplasms of Bartholin's glands. Wide excision in early cases, radical vulvectomy in largely progressed carcinoma and radiotherapy for inoperable cases are the methods of procedure. The period of survival after operation appears to be restricted to a few years, even when radical excision has been combined with post-operative Roentgen irradiation.

Infections of Skene's Ducts

Occasionally another form of pseudoabscesses of the vestibulum vulvae may give rise to diagnostic considerations. As the accessory ducts of the male urethra, so also the *paraurethral ducts*, and especially *Skene's ducts* of the female are accessible to gonococcal and rarely to non-gonococcal infection. This complication may escape attention for a long time, the infected ducts remaining sources of continual reinfection.

Due to chronic obstruction of the inflamed ducts of Skene and the accumulation of pus, peri- or paraurethral pseudoabscesses may develop increasing in size up to the size of a cherry, mulberry or plum. Occasionally

larger paraurethral infiltrations may form extending toward the labia minora or the lowest portion of the vagina. The reader is referred to Huffman s study in *Am J Obst & Gynec* 55 1948.

A fully developed abscess of Skene s duct is reproduced in Figure 139 Swelling and infiltration of the involved vulvar tissue have dislocated the orificium urethrae which is visible as a narrow slit as marked by arrow



FIGURE 139 Abscess of Skene s duct. (Dermat Clinic, Frankfurt, Prof Dr O Gans.)

Differential diagnosis: The infiltrative form of infection of Skene s ducts may give rise to diagnostic errors Extensive and deeper infiltration may protrude the vestibular mucosa in such a manner as to simulate a malignant neoplasm without any symptom indicative of an infectious process.

Treatment: Pseudoabscesses of Skene s ducts require the same treat ment as do those of Bartholin s glands Surgical procedure is the method of choice

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CHAPTER 19

NONVENEREAL DISEASES OF THE TESTIS EPIDIDYMIS AND SPERMATIC CORD

A. Introduction
B. Orchitis Traumatica, Orchitis Erotica
C. Torsion of the Spermatic Cord
D. Orchitis in Cryptorchism
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A Introduction

The differentiation of venereal and nonvenereal diseases of the testis and epididymis presents difficult diagnostic problems Orchitis occurs as a complication of systemic bacterial or virus infections (metastatic orchitis in mumps grippe, brucellosis, etc.) in systemic fungus infections or in association with allergic conditions such as serum sickness. Malignant growth may produce swellings easily mistaken for syphiloma of the testes

Nonspecific epididymitis is a condition, due to bacillary infection from the urethra, seminal vesicles or the prostate or it may develop after trauma, occasionally as an unwelcome sequel to instrumental or surgical treatment. Chronic inflammatory residues give rise to diagnostic difficulties. Kocher was one of the first to emphasize the fact that many cases diagnosed as chronic epididymitis eventually proved to be tuberculosis. Other cases however although clinically typical of tuberculous epididymitis when operated upon, showed nothing but indifferent inflammatory changes in the removed tissues.

Kocher's classical distribution of the inflammatory diseases of the testis and epididymis into three groups, namely traumatic, urethral and metastatic forms, has been repeatedly modified in the course of modern progress but still offers a suitable basis for the purpose of our description An additional group designated in the literature as idiopathic orchitis

encompasses all cases of obscure origin. The number of the latter has however been greatly reduced as a result of recent research.

B Orchitis Traumatica

Orchitis may develop following almost any injury to the scrotum such as a simple contusion, a fall astride some hard object a saddle injury a kick by a horse, or a blow from a batted baseball. Frequently both testicles are involved, with or without damage to the epididymis.

Simple trauma is not necessarily followed by rupture of the testes and of hematoma of the tunica vaginalis, which are more common following penetrating gunshot wounds. Severe injury may dislocate the testes. Chronic hydrocele is a common sequel to traumatic orchitis. Partial or total atrophy is often the end result of traumatic injury As a rule the accident is followed immediately by temporary shock, nausea and vomiting Collapse is less frequent when the tunica vaginalis has been torn Injury of the testicle may leave a "locus minoris resistentiae" favoring secondary bacillary invasion. The role of trauma in the pathogenesis of nonspecific epididymitis will be discussed in the pertinent section

Treatment

In cases of simple trauma, a strictly conservative attitude is indicated. However when hematoma of the tunica vaginalis is evident, early incision has been advocated. At all events orchidectomy should not be performed hastily

In addition to direct trauma, a continuous concussion of the scrotum may cause slight to moderate enlargement of the testicles in chauffeurs, motorcyclists or horseback riders, the pains being usually mild, but tender ness to touch being marked.

Waelsch's "*orchitis erotica* attributed to sexual congestion following prolonged abstinence represents a simple increase in volume rather than an inflammatory condition. The spermatic cord is never involved and spon taneous regression within a few days is the rule

Orchite par effort" has been described by French authors as a special type of traumatic orchitis developing after a sudden violent contraction of the cremaster or the abdominal muscles. Many of the reported instances, however were probably secondary to torsion of the spermatic cord

C. Torsion of the Spermatic Cord

This condition presents differential diagnostic difficulties especially in children It has been observed even in newborn infants, but is not un common in adults between fifteen and twenty five years of age In the majority of cases, congenital anomalies play an important role in torsion

of the testicle, especially an improperly descended testis. The widely accepted hypothesis that a violent muscular strain is primarily responsible for torsion of the cord cannot be maintained, since adults have been surprised by a sudden onset of symptoms during sleep Excruciating pains, rapid swelling, nausea, vomiting, a high pulse rate and fever indicate a serious condition. Spontaneous detorsion is possible, but relapses may occur Usually there is little time for an expectant attitude, and an early diagnosis is imperative. Circulatory obstruction will soon result in edema of the cord, accumulation of fluid in the tunica vaginalis and possibly gangrene.

The true origin of torsion of the spermatic cord is still uncertain. The cord and testicle may be turned around the vertical axis of the cord from 180° to 360° even two or three revolutions have been found at operation. Torsion may also occur bilaterally

Differential Diagnosis

The most common diagnostic error especially in children is a misinterpretation of the condition as an acute hematogenous orchitis or urethrogenous bacterial, nonspecific orchi-epididymitis. An incidental presence of a urethral discharge in adults should not be considered too decisive in diagnosis. In cases of combined undescended testis and congenital inguinal hernia, the symptoms may easily be mistaken for incarcerated hernia.

Treatment

Surgical intervention is definitely indicated, unless spontaneous detorsion occurs within a limited observation time When performed during the first four hours following onset of symptoms, surgical detorsion may save the testicle and prevent partial or total atrophy Possible relapse can, as a rule be prevented by suturing the testicle to the septum and the parietal tunica at the base of the scrotum, (orchipexy) Once gangrene has set in, orchidectomy becomes imperative

Much less common than torsion of the spermatic cord, is the torsion of *Morgagni's hydatid* a non-pedicled rudimentary structure adhering to the head of the epididymis. In this condition clinical symptoms develop less rapidly and are milder than in torsion of the cord

D Orchitis in Cryptorchism

Orchitis due to torsion of the spermatic cord is not the only form of inflammatory disease of an undescended testicle External injury may suffice to cause a traumatic swelling of the arrested organ. In addition

bacterial orchitis may involve the undescended organ by hematogenous or urethral infection Then the clinical symptoms are like those in the ordinary forms of bacterial orchi-epididymitis When cryptorchism is combined with a congenital inguinal hernia, a mistaken diagnosis of incarcerated hernia is possible if the observer fails to note that the corresponding half of the scrotum is empty

Treatment

In the majority of cases removal of the arrested organ is indicated, since the latter is usually already doomed to atrophy Prophylactically early orchiopexy or hormone therapy have been advocated to prevent all possible complications of a lasting cryptorchism. It should be remembered also that the undescended testis is particularly prone to undergo malignant transformation

E. Urethral Non-gonococcal Orchitis and Epididymitis

Inflammatory enlargements of the epididymis of urethral origin are always bacteriogenic. They develop when pathogenic bacteria have found their way through the vas deferens into the epididymis from the posterior urethra, the seminal vesicles the prostate, or primarily from any portion of the upper urinary tract

Bacterial epididymitis often develops as an unwelcome side effect of instrumental or surgical procedures such as catheterization or prostatic surgery It is not infrequently a sequel of prostatectomy delaying or impairing recovery In an effort to prevent this complication, vasectomy is now generally done preceding prostatectomy

Abscess formation is not infrequent in nonspecific bacterial epididymitis, and may involve the testis. Chronic changes lead to indurations of the epididymis which often harbor the infectious agents for a long time.

The *pathogenesis* of epididymitis has long been a subject of general discussion. Clinical experience and experimental observations suggested, that the antiperistaltic contractions of the vas deferens constitute an essential factor in the transportation of infectious material from the urethra into the epididymis It was believed that muscular contractions of the vas deferens might be released *by mechanical and nervous irritations as well.* Even relatively slight concussions appeared sufficient to produce bacterial epididymitis.

This hypothesis offered an explanation of the epididymitis following catheterization or surgical procedures that might cause a mechanical irritation of the vas deferens It also seemed to explain the fact, that not every epididymitis is preceded by an infectious deferentitis. W Frey however could not find a sufficiently conclusive or definite proof in any of the

respective communications that there positively exists any peristalsis or antiperistalsis of the vas deferens. In his own experiments, in many animals, he observed no such movements. He assumed that the morbid process more likely progresses by continuity from the seminal vesicles to the epididymis, even though anatomical changes in the vas deferens may not be demonstrable. He also points to the possibility of a lymphatic route of the infectious process along the cord.

Rolnick, in his Practice of Urology (1949) suggested that initially the respective bacteria pass rapidly along the lumen of the vas deferens to the epididymis without involving the vas itself but that once a bacterial epididymitis is fully developed, the vas is eventually involved, sometimes in its entire length.

The question as to whether or not the vas deferens is functionally capable of propelling urethral contents into the epididymis by muscular contraction, remains a problem for further investigation.

The *clinical symptoms* of acute non gonorrheal epididymitis do not differ essentially from those of acute gonococcal epididymitis The course, however may be more or less determined by the type of the infectious micro-organism, which has been identified in specimens of the aspirated material from the affected organ. Conclusive findings of such organisms, however are not the rule.

The great multitude of bacteria, which may invade the epididymis from the posterior urethra has been described in Chapter 17 on non gonorrheal urethritis. Severe cases with high fever considerable swelling and edema, with or without involvement of the testicle, deferentitis and serous periorchitis may occur Abscess formation is more common in non gonococcal than in gonococcal epididymitis. Rapidly developing circumscribed abscesses frequently go on to spontaneous rupture

Many cases of nonspecific epididymitis run a subfebrile or afebrile course, with only a slight or moderate swelling However chronic nodular infiltrations may persist, located predominantly in the head of the epididymis—a starting point for possible relapses. Clinically these residual infiltrations frequently constitute a source of difficulty in the differential diagnosis from tuberculosis.

The histological findings in nonspecific epididymitis and epididymo-orchitis include inflammatory changes, such as perivascular infiltration, hypertrophy of the connective tissue, partial destruction of the seminiferous tubuli of the testes and of the efferent tubuli of the epididymis.

Differential Diagnosis

Of foremost importance is the differentiation between *nonspecific* and *tuberculous* epididymitis, that will be discussed in the following section.

The possibility of a chronic residue from gonorrheal epididymitis must be excluded by all diagnostic methods. A history of earlier gonorrhea will not justify the assumption of a post-gonorrheal process and would not exclude the possibility of a subsequently acquired nonspecific epididymitis

Syphilis involves chiefly the testicle, rarely the epididymis. *Orchitis syphilitica* develops slowly and without pain. If both the testis and epididymis are affected, a characteristic pear shaped, solid tumor results, with a smooth surface Exceptionally bilateral syphilitic orchitis has been observed. Primary syphilitic epididymitis is extraordinary The evaluation of positive serologic tests must be made with reservations owing to the possibility of the development of a nonspecific epididymitis in a patient with seropositive latent lues.

Metastatic orchiepididymitis differs from the urethral form of nonspecific urethritis by the primary involvement of the testis *Malignant neoplasms* proceeding from the testicles may involve the epididymis. The resulting tumors, however differ from nonspecific epididymitis by their progression and corresponding changes in shape and consistency as well as by involvement of the regional lymph glands.

In the *treatment* of nonspecific epididymitis the symptomatic therapy differs little from the methods in general use for gonorrheal epididymitis and includes bed rest, heat and suspensory bandages combined with analgesic medication. Incision and drainage of large abscesses are indicated. Instrumentation should be avoided. Autovaccine injections have proved effective, especially against B coli infections. Of primary importance however is the modern treatment with sulfonamides and antibiotics Selection of the particular compound and its dosage must be based on the bacterial agent responsible in the individual case and on the particular antibiotic spectrum of the various compounds in question

F Epididymitis and Epididymo-orchitis Tuberculosa

As a rule genital tuberculosis in the male is a secondary condition derived from tuberculosis of the lungs the peribronchial lymph glands, or from any other primarily infected part of the body The genital infection often develops in association with tuberculosis of the uropoietic system (urogenital tuberculosis) However both tuberculosis of the genital and the urinary organs may develop separately Autopsy findings have demonstrated that the tuberculous process can remain confined to the genital organs for an undetermined time with no changes in the urinary tract and vice versa.

Tuberculous infection of the epididymis provides the starting point for genital tuberculosis, just as hematogenous infection of the kidney does in tuberculosis of the urinary organs. Predominantly the tail of the

epididymis is the site of such infection, less frequently the body of the organ whereas nonspecific epididymitis usually involves the head of the epididymis.

Evidence has been produced that the morbid process can remain limited to the epididymis for a long time without involving the testicle. Epididymo-orchitis tuberculosa develops rather late. Bilateral epididymitis has been occasionally observed in advanced cases of chronic tuberculosis. Intervals of months or years have been noted until the involvement of the previously intact organ of the opposite side became manifest. Bilateral tuberculous epididymitis is very rare

An insidious onset little or no pain slight tenderness on pressure, slight to moderate elevations of the body temperature a firm nodular swelling in more advanced cases, abscess formation are characteristic of genital tuberculosis of the male.

In the majority of cases tuberculous epididymitis runs a chronic course, frequently extending over years. The genito-primary infection may remain undetected even for decades until the latent focus becomes active. Then a rapid progression may set in including the testicle, vas deferens, seminal vesicles and prostate, often complicated by manifestations of tuberculosis of the urinary tract. Fever emaciation, involvement of other organs and secondary infections darken the prognosis in such florid cases.

However even after activation of a hitherto latent focus in the epididymis, resting periods are possible also in untreated cases.

An explosive turn for the worse occurs especially in connection with intercurrent diseases such as measles, grippe, scarlet fever diseases of the metabolism, or in cases of malnutrition or after trauma.

Pathogenetically the concept of a testifugal" progression of the morbid process has been generally established. However the possibility of a testipetal" route, i.e., progression in a direction opposite to that of the secretory flow cannot be definitely excluded. In some cases where genital tuberculosis develops secondary to tuberculosis of the urinary organs the prostate or the seminal vesicles may harbor the "genito-primary" infection. In addition, the possibility of a lymphatic spread of infection, especially from tuberculous lymph glands, must be taken in consideration

Differential Diagnosis

The differential diagnosis between epididymitis tuberculosa and non specific epididymitis, so important for an early treatment of genital tuber culosis, presents an intricate problem to surgeon urologist and general practitioner In every unclear chronic enlargement of the epididymis, even if inconspicuous, or occurring in otherwise apparently healthy individuals, the possible presence of a tuberculous process must be considered. On the

other hand there occur instances of chronic epididymitis of a non tuber culous origin presenting a combination of symptoms similar to those of tuberculous epididymitis

In the past, when the majority of the clinical symptoms seemed to indicate tuberculosis, epididymectomy was usually performed. In spite of careful clinical examinations it happened that histologically merely uncharacteristic inflammatory symptoms were found in stained tissue specimens, with no tubercles epithelioid or giant cells. Evidence has been produced by pathologists and urologists that incidentally tuberculous infec tion may cause only inflammatory tissue changes without the formation of typical tubercles (Landouzy and Gougerot, Suren, Wildbolz, Harkins) Chronic inflammation without tubercles has been noted also in tuberculosis of other organs as for instance in tuberculosis of the skin or the joints

Wildbolz, in a patient with typical symptoms of tuberculous epidid ymitis found no tubercles or giant cells in histologic studies but, in some sections numerous Koch bacilli were seen in the interstitial tissue and in the lumina of the canaliculi In other cases, even in the absence of bacil lary findings animal inoculation has revealed the presence of bacilli in an inoculum prepared from the tissue of the epididymis In addition Zurhelle was able to demonstrate Koch bacilli in tissue of apparently normal epididymides of two otherwise tuberculous individuals. Possibly these findings illustrated the earliest stage of bacillary invasion of the epididymis.

Treatment

All these findings justify the expectant attitude advocated by many surgeons in uncomplicated cases of epididymitis of possible tuberculous origin, especially if neither the history nor the results of general examina tion yield additional data indicative of tuberculosis. Wildbolz strictly rejects even biopsy as a diagnostic aid in uncertain cases the opening of a hitherto closed focus of infection may prove detrimental by spreading the infection

Other surgeons however have warned against too long a postpone ment of epididymectomy even in doubtful instances lest the chance for prevention of involvement of the testicle in a possible tuberculous process, be lost. The advocates of this method of procedure emphasize that even in nonspecific forms of chronic epididymitis, the chronic inflam mation and the resulting sclerotic changes interspersed with minute foci of suppuration in the affected tubuli will hardly permit any restoration of permeability for spermatozoa. For this reason this group of surgeons believe that the risk of a possibly unnecessary extirpation of such an epididymis must be considered of minor importance prompt epidid

ymectomy performed in time usually yields excellent results in epididymitis tuberculosa.

Once the testicle has been involved in the pathologic process, orchiepididymectomy becomes imperative.

G Orchitis and Epididymitis Leprosa

The involvement of the genital organs is common in leprosy It occurs already in the early stages of the disease. As a matter of fact, the testes and epididymides are no less frequently involved than the liver and spleen in this disease.

Autopsies reveal foci of infection in the genital organs in the majority of cases It appears that the tissues of the generative organs are particularly susceptible to infection by the Hansen bacillus. Bacilli are demonstrable in the tissues of the testis and epididymis, and occasionally in the seminal ejaculate. This may explain the fact, that male lepers become impotent very early Azoospermia and aspermia develop rapidly Bilateral involvement of the testes and epididymides is common Grabstald and Swan (1952) found atrophy of the testes in 28 per cent of a series of one hundred and seventy-nine male lepers Gynecomastia had developed in 19 per cent of the cases.

Also in females the ovaries may become involved in the early stages of leprosy Pregnancy in a leprous woman usually but not necessarily ends in abortion Bacilli will be found in all organs of the fetus.

Not infrequently leprosy develops in children and adolescents If the genital organs become involved before puberty sexual maturation is inhibited.

Histology

Orchitis leprosa presents a characteristic picture with infiltration of the vascular walls and the adjacent tissues by the Hansen bacillus inter stitial cell clumping and atrophy of the seminiferous tubules, progressing to complete fibrosis and obliterating endarteritis (Grabstald and Swan)

To date, the *mode of transmission* of leprosy has not been clearly established. However the conception prevails that infection depends upon a close personal contact over a long period of time (as in bed partners) and is transmitted via the skin or the nasal and pharyngeal mucous membranes (Kluth, 1951)

The *differential diagnosis* must include in particular tuberculosis and syphilis of the epididymis and testicle In differentiation of leprosy from syphilis it should be kept in mind that positive Wassermann reactions have *occasionally been noted in non-syphilitic lepers.* Tuberculosis

may develop secondarily in the later stages of leprosy and thus may be superimposed upon a leprous infection of the testis and epididymis.

The treatment of leprosy is thoroughly discussed in the literature.

H Metastatic Orchitis and Epididymitis in Acute Infectious Diseases

Orchitis in Mumps	Infectious Mononucleosis
Orchitis Grippalis	Glanders
Typhoid Orchitis and Epididymitis	Typhus
Brucella Orchitis and Epididymitis	Q-Fever
Septicemic Orchitis and Epididymitis	Malaria Orchitis
Pneumonia	Variola Orchitis
Angina	Varicella
Rheumatic Fever	Dengue Fever

Hematogenous (metastatic) orchitis occurs in numerous acute systemic infections, such as mumps influenza, typhoid, or secondary to focal infection elsewhere in the body (angina, osteomyelitis) The inflammation is limited primarily to the testicle, but occasionally involves also the epididymis. In many instances the pathogenic micro-organism can be demonstrated microscopically and by culture in the aspirated testicular material. One or both testes may be affected.

The onset is sudden associated with pain, swelling and fever The pathologic findings show no essential difference in the various types of metastatic orchitis. *Histologic* changes vary from interstitial round cell infiltration to severe tubular lesions and degeneration of the spermatogenic cells Focal necrosis and minute abscesses (micro-abscesses) are characteristic of hematogenic orchitis larger abscesses may develop Extensive suppuration may lead to atrophy and azoospermia. In the majority of cases however metastatic orchitis goes on to resolution and as a rule runs a benign course extending over several days up to two or three weeks

Opinions may differ in an individual case as to whether the inflammation of the testicle is metastatic or is derived from infections of the urethra, prostate or the upper urinary tract. Thus for instance, in typhoid epididymo-orchitis it may be difficult to decide whether the involvement is due to excretion of the typhoid bacilli in the urine or to hematogenic bacillary invasion.

Metastatic orchitis has been produced experimentally by the injection of bacterial matter as well as of bacterial toxins into the afferent blood vessels of animals (Fraenkel and Hartwich)

Hematogenous orchitis develops either after the onset of general symptoms i.e during the febrile period or during convalescence. Metastatic orchitis has been known to develop as late as three or four weeks after defervescence often causing renewed attacks of fever Such late manifestations often give rise to diagnostic difficulties.

Differential Diagnosis

Orchitis developing during the period of convalescence demands *differentiation* from urethral forms of orchitis The incidental presence of some indifferent discharge must not be taken as any conclusive diagnostic feature. As a rule gonococcal epididymitis does not involve the testicle. The presence of suppuration will demand diagnostic exclusion of tuberculosis. Tuberculosis begins usually in the tail of the epididymis, producing a painless, roundish, firm nodule and may be discovered incidentally Syphilitic orchitis causes a chronic, painless, diffuse and predominantly unilateral induration.

The following survey will indicate the multitude of acute systemic infections that may give rise to metastatic orchitis.

(1) Orchitis in Mumps

Orchitis in *mumps* is the most common type of hematogenic orchitis, and is also one of the most common complications of that disease. It occurs very rarely before puberty and is usually observed in patients between eighteen and forty years of age. Based on large-scale statistics, it has been estimated that orchitis develops in about 25 per cent of all cases of epidemic parotitis, the incidence varying with the severity of the epidemic. Unilateral orchitis is the most common type. The epididymis is rarely involved. The inflammation of the testicle usually develops within the first six days after the onset of parotitis, but occasionally precedes the swelling of the parotid gland. In the course of widespread epidemics, orchitis has been known to occur in the absence of any demonstrable changes in the parotid glands in men intimately exposed to the infection (as in a case of Danielson, in which orchitis without parotitis developed in a married man during a familial epidemic affecting the wife and six children)

Abscess formation is uncommon in mumps orchitis. However in cases of bilateral orchitis, atrophy and sterility may result. Postmortem examinations in such cases revealed extensive round cell infiltration associated with interstitial serofibrinous exudation, tubular damage, focal necrosis and degeneration of sperm cells (Manca) Reuscher examined testicle material from a youth of eighteen years, who had suffered from mumps orchitis four years before his death. The whole testis was shrunken and hemorrhagic infarction due to thrombosis was still evidenced by pigmentation within the atrophic tissue

Treatment: Bed rest is strongly recommended. However R. E. Smith found that in nine out of twenty-five patients with mumps, confinement to bed from the first day did not prevent the development of orchitis. The

latter occurred less frequently in patients given convalescent serum intravenously on admission. Surgical procedure has been advocated to relieve pain and to prevent further swelling of the testicle with resulting major damage to spermatogenesis After incision of the tunica vaginalis a secondary hydrocele promptly empties and the intratesticular edema will be reduced. Many authors, however are of the opinion, that puncture and aspiration will suffice to shorten the course of mumps orchitis Some clinicians do not believe in the preventive effect of surgical intervention assuming that it is the toxic influence of the virus rather than mere pressure due to intratesticular edema, that is responsible for the lasting damage

Recently French authors inaugurated the treatment of mumps orchitis with *diethylstilbestrol*, 1 mg. of estrogen three times daily for five successive days Even a total of 4 mg. a day was well tolerated with no undesirable side-effects Savran (1949) in a series of one hundred and seventy-seven cases of mumps reported orchitis as occurring in only 3 9 per cent of the treated patients In a control series of one hundred and sixty-eight cases in which no estrogen was administered, the incidence of orchitis was 16.6 per cent A. Hogue *et al* reported beneficial effects of this treatment also in already developed mumps orchitis with a definite shortening of the course. This mode of therapy is based on the idea of bringing the testicle back to the state of puberty before which period mumps orchitis rarely develops

(2) Orchitis Grippalis

Orchitis and epididymitis are less uncommon as complications of influenza than might be judged from the reports in the literature. Orchitis usually develops during the initial febrile period, whereas epididymitis is more common during convalescence, following cessation of fever In this late type of genital involvement, differential diagnosis from infections of the urethra and of the upper urinary tract will be required.

Occasionally patients may complain of a painful swelling in the scrotum, having had no previous exposure to gonorrheal infection, nor even recollection of a cold in preceding weeks. No urethral discharge is present and bacteriologic examination of scrapings from the urethra proves negative In such cases a careful study of the anamnesis will finally give the clue to the etiology Recovery usually takes place in from five to six days up to two or three weeks

(3) Typhoid Orchitis and Epididymitis

The testis and epididymis are rarely involved in typhoid fever Osler in a review of fifteen hundred cases of typhoid reported only four cases of epididymitis Recent reports show a higher incidence Greenberg and

Greenwald, in a series of eighty-eight cases of typhoid epididymitis recorded that in seventy-one instances the complication developed during convalescence and in seventeen instances, during the febrile climax of the disease. Abscess formation occurred in about 20 per cent of all cases. Early incision has a palliative effect. Typhoid bacilli have been demonstrated in the pus, with or without concomitant bacteria. Positive Widal reactions have been obtained from the aspirated punctate in epididymitis typhosa. Infection from the urinary tract is the rule but unequivocal hematogenous orchitis has been described.

(4) Brucella Orchitis and Epididymitis

Orchitis occasionally develops as a complication of infection with brucella melitensis (Malta fever) Severe orchitis, associated with periorchitis, prostatitis and deferentitis have been reported. The orchitis associated with brucellosis is said to be characterized by a long course. The morbid process usually includes the epididymis. In suppurative epididymo-orchitis, bacteriologic examination will yield positive proof of brucella melitensis infection.

(5) Septicemic Orchitis and Epididymitis

Metastatic orchitis and epididymitis are known to occur in staphylococcic and pneumococcic septicemia (Dumont and Tissier) especially in systemic infection derived from osteomyelitis. Lombard described orchitis caused by general septic infections in two nurslings, in one orchitis without epididymitis, and in the other epididymitis without orchitis. The incidence of septic infection of the genital organs in newborn infants has long been questioned in most of the case reports it was ascribed to a preceding trauma or to torsion of the cord.

(6) Pneumonia

Reports of genital complications in pneumonia are scarce. Serri found the pneumococcus Friedländer in the aspirated material from orchitis in two cases of pneumonia and the microscopic findings were substantiated by culture In the one patient a purulent orchitis developed in the other the epididymis was primarily involved. Both patients responded to sulfonamide therapy

(7) Angina

Orchitis in connection with angina or other inflammations of the pharynx has been described by French authors as orchite amygdalienne Campbell observed acute orchitis in an infant with streptococcal angina. Schober reported a case of orchitis in a baby of one and one-half years,

developing on the twelfth day of retropharyngeal abscess. A walnut-sized swelling receded within four days.

(8) Rheumatic Fever

Orchitis rheumatica resembles mumps orchitis. Bilateral orchitis with periorchitis leading to atrophy has been reported In three instances reported by Bogdan the swelling of the testicle preceded the onset of polyarthritis.

(9) Infectious Mononucleosis

A swelling of the testis developing during the early stages of infectious mononucleosis may be mistaken for a grippe orchitis. This error is understandable considering the initial symptoms of infectious mononucleosis including fever tonsillitis or pharyngitis and the absence of enlarged lymph glands and spleen in the early stages Characteristic blood changes are not necessarily demonstrable in infectious mononucleosis before the febrile period is well over Swelling and pains are slight to moderate, but even cases with slight swelling may result in atrophy Mackay Dick, in one of several such patients noted complete atrophy of the left and, at the same time a progressive swelling of the right testicle.

(10) Glanders

In *glanders* the testis is a selective localization of metastatic orchitis Malleomyces mallei, or m. pseudo-mallei, are easily demonstrable in the testicular punctate Malleus orchitis has been induced experimentally in guinea pigs by intraperitoneal injection of infected tissue or of nasal secretion from human patients. In these animals, orchitis developed rapidly associated with general spread of the infection. This model experiment has been established as a reliable diagnostic test in dubious cases of human infection

(11) Typhus

Metastatic orchitis in *typhus* is most destructive. Morgenstern found marked tissue changes enlargement of Sertoli's cells decrease in lipoid contents of Leydig's cells and damage to the sperma cells many histiocytes were seen, most probably derived from the connective fibers of the canaliculi

(12) Q-Fever

Epididymo-orchitis has been observed after defervescence in *Q fever* (Queensland fever caused by Rickettsia brunati) Clinically resembling

orchitis grippalis, this painful complication develops rapidly to recede gradually within fifteen to thirty days (Korting)

(13) Malaria Orchitis

Malaria orchitis (the orchite paludéenne of the French authors) has been described by di Pace, di Roma and recently by Zedda. Da Rin observed acute orchitis following malaria treatment of a fifty three year old paretic. The orchitis persisted for three or four days and then regressed rapidly under quinine therapy

(14) Variola Orchitis

Variola orchitis usually results in atrophy

(15) Varicella

Orchitis in *varicellae* although very rare, has been observed in unequivocal cases by Sabrazès and by Rouèche. The first author s patient was twenty two years of age Rouèche s case occurred in an infant. Wesselhoft and Pearson described orchitis and epididymitis in a forty six year old man who had been exposed to chicken pox infection during a familial epidemic. The testicular affection was followed by partial atrophy another complication was pneumonitis.

(16) Dengue Fever

Orchitis in *dengue fever* was studied during the War in the South Pacific. A very late onset, sometimes after a period of months, appears to be characteristic. Weyrauch and Gass reported five cases of orchitis in a series of one hundred and forty-one soldiers suffering from dengue fever in three of these five cases, the orchitis was bilateral. Bloody seminal emissions have repeatedly been described in connection with dengue fever

I. Orchitis Due to Systemic Fungus Infection

Sporotrichosis	Coccidioidomycosis
Actinomycotic Orchitis	Blastomycosis

Sporotrichosis, actinomycosis and blastomycosis are known to produce metastatic orchitis. Nothwithstanding the increasing number of reports in the world literature our knowledge of these conditions is incomplete. In the majority of cases, the mycotic origin of the testicular swelling was detected incidentally at autopsy or in connection with prostatectomy for carcinoma of the prostate It was almost never possible to determine the primary focus of fungus infection Frequently the nodular or diffuse in-

durations of testis and epididymis were mistaken for malignancy or tuber culosis.

Experimentally mycotic orchitis can be reproduced in animals by intratesticular or intraperitoneal injection of cultures from aspergillus fumigatus, actinomyces bovis cryptococcus hominis and trichosporium Mantegazza (Chiurco Sanazzari) Histologic examination will then reveal a granulomatous orchitis with focal necrosis suppuration sclerosis and atrophy Mycotic elements are found in the pus as well as free in the parenchyma.

Sporotrichosis

In *human sporotrichosis* epididymo-orchitis may easily be mistaken for tuberculosis Beginning as a nodular swelling, a chronic condition develops *with or without pains and fever* Even in the absence of other clinical symptoms of tuberculosis, the latter disease has often been suspected and early epididymectomy was performed in several cases (Petrignani, Lafaille and Pavie *et al.*) Microscopic examination, however revealed no evidence of tuberculosis but many macrocytes, harboring fungi, were observed in the inflamed areas and conidia were found freely distributed in the affected tissue Cultures revealed the sporotrichum of Beurman. The picture resembled that of granulomatous orchitis developing in experimen tally infected rats. In several instances, cutaneous sporotrichotic ulcers were present as an additional symptom of fungus infection.

Coccidioidomycosis

Urogenital lesions are very rare in *coccidioidomycosis* The few observations of recent times show that also the coccidioidal granuloma of the testis and epididymis may mimic tuberculosis Rohn Davila and Gibson described this condition as a secondary manifestation of disseminated coccidioidomycosis

Actinomycotic Orchitis

Actinomycotic orchitis has usually been detected incidentally in orchidectomy specimens. D H. Schneider and also Baker and Ragius were thus surprised to find ray fungus colonies in the pus of focal abscesses in such material. In other instances actinomyces granula were found in testicles extirpated for adenocarcinoma of the prostate The enlargement of the testicles had been ascribed to propagation of the malignant tumor

Blastomycosis

Blastomycosis (Gilchrist s disease) may occasionally involve the genital organs. Moore and Halpern described a fatal systemic infection with

zymonema dermatitidis, the fungus usually causing North American blastomycosis, in a physician of fifty-four years of age Clinically cough with expectoration of a grayish bloody sputum, dysuria, excessive enlargement of the prostate and the epididymis, indicated a serious systemic infection. Postmortem examination revealed purulent prostatitis, vesiculitis, epi didymitis and a serious involvement of the lungs and adrenal glands Fungi were found in abundance in all tissues examined.

Eisenstaedt and Boughton described orchitis prostatitis and vesiculitis associated with multiple cutaneous lesions in generalized blastomycosis. Of four patients observed by Jacobson and Dockerty one presented skin lesions and epididymitis without involvement of the prostate another patient showed orchitis and epididymitis associated with a discharging scrotal sinus.

J Acute Orchitis in Tropical Diseases

Filaria Bilharzia Orchitis

Filaria

Involvement of the genital organs was not uncommon in soldiers ex posed to *filaria* infection in the South Pacific during World War II Large numbers of larvae entering the lymph and blood vessels found their way into the tissue with resulting funiculitis, and epididymo-orchitis with edema, hydrocele, *varicocele, lymphangitis, lymphadenitis and scrotal involvement.* In such cases, a painless swelling and edema of the spermatic cord usually persists for a long time, without any swelling of the epididymis. Suppura tion rarely occurs.

Orchitis due to filariasis is characterized by spongy edematous con sistency The history may in an individual case reveal the etiology How ever soldiers transferred to a temperate climate were frequently unaware of some thickening of the cord. The affection was detected incidentally and had often given rise to diagnostic errors (Coley and Lewis)

The *differentiation* from tuberculosis is of foremost importance. Tuber culosis begins with a painless firm nodule in the upper pole of the epi didymis and tends to caseation Gonococcic epididymitis and deferentitis are acute painful conditions, associated with urethral discharge Syphilis affects the body of the testis rather than the epididymis the cord is rarely involved. Marks described filaria funiculitis causing a cystic pedunculated swelling simulating an epiploic hernia.

Bilharzia Orchitis

In bilharziasis, bilateral orchitis tending to abscess formation and fistulization is not uncommon. The purulent secretion contains countless

eggs Eggs may also be demonstrable in the sperma of bilharzia patients, originating from the prostate the seminal vesicles the testis or epididymis (*ovispermia bilharzica, Pfister*) *Bilharzia epididymo-orchitis* resembles tuberculosis. It may develop either by direct invasion or hematogenic dis semination of schistosoma haematobium. Genital bilharziasis may be com plicated by secondary bacterial infection from the urethra.

K. Infarction of the Testicle

In 1924, H Kuttner directed attention to the incidence of acute rapidly progressing destruction of a previously intact testis in otherwise healthy individuals. Similar cases were reported by Mulzer and Buschke Grund, Esau, and more recently by Cedermark, Knudtson and de Surra Canard.

The afflicted patients were twenty to thirty years of age. Gonorrhea did not appear in the anamneses Neither trauma nor general infections had preceded the sudden onset of pains and the inflammatory swelling of the testicle, epididymis and spermatic cord. Usually orchidectomy was per formed. Severe inflammatory changes were found, with a constant finding of thromboses of small arteries veins or capillaries

The pathologic changes were the same as those caused by obstruction to venous drainage in experimental or surgical interruption of the cir culation in the pampiniform plexus Venous thrombosis of the pampiniform plexus whether of primary or secondary origin produces a condition of stasis in the testis which may lead to the type of total hemorrhagic infarction, known as congestive infarct (Cedermark) Occasionally this condition may develop after varicocelectomy In *Knudtson s case*, *opera tion* revealed an atrophic left testicle, with a brownish-yellow discoloration of the parenchyma, necrosis of the seminiferous tubuli and stroma cells due to infarction of the entire testicle. There was an extensive thrombosis of the plexus pampiniformis

Differential Diagnosis

The clinical symptoms of infarction of the testicle hardly differ from those caused by torsion of the spermatic cord. However torsion of the spermatic cord is associated with high fever vomiting and ileus all of which symptoms are lacking in infarct of the testicle The differentiation may be difficult, especially in patients with a history of earlier attacks of torsion of the cord.

Treatment

For a long time, orchidectomy was strongly recommended for infarct of the testicle However cases have been reported in which the tendency

to progression was less marked, resulting in only a partial destruction of the parenchyma. Puncture of the tunica vaginalis for the purpose of emptying a concomitant hydrocele before proceeding to radical surgery has been recommended. Early orchidectomy involves the risk of removal of functionally intact tissue.

L. Orchitis as an Anaphylactic Phenomenon

Attention must be drawn to the occasional swelling of one or both testicles as an anaphylactic phenomenon following serum injections in acute infectious diseases If serum sickness is not manifested by a skin rash and muscular or articular pains, diagnostic errors may easily occur Carrien observed a bilateral orchitis on the twelfth day and Nogues orchitis on the eighth day after injection of antidiphtheritic serum (orchiépididymite serique) In an infant suffering from nasal and pharyngeal diphtheria, Goodall observed swelling of the testicles after several serum injections. Following the first injection an urticarial reaction was noted at the site of injection Guinon and Lamy described orchitis in two boys of six and one-half and eleven years of age eight days following serum treatment for cerebrospinal meningitis In both patients regression followed after forty eight hours Schiavone reported orchitis five days after revaccination of an infant. The first vaccination, at the age of two years, was not followed by any rash or other side reactions.

M Epididymitis Eosinophilica

This rare condition occurs as a secondary symptom in the eosinophilic infiltrate of the lungs, which clinically simulates focal pneumonia. The disease is characterized by the large number of eosinophils in the cellular contents of the infiltrated areas (60 to 70 per cent, von Meyenburg) Local eosinophilia is always associated with an *increase* of *eosinophils* in the circulating blood. This condition has been interpreted as an allergic reaction of the lungs to various antigens.

One of the first to describe epididymitis as a syndrome of the lung infiltrate, was Meyenburg It was natural that the first cases observed of this combination of pulmonary symptoms with swelling of the epididymis were mistaken for tuberculosis. Early epididymectomy appeared indicated. *Histologically* however there were no signs of tuberculosis the picture resembled rather that of nonspecific epididymitis, except for the striking accumulation of eosinophils in the tissue. Eosinophilia of the blood was always present.

Mettler confirmed these findings in a review of nine cases of epididymitis eosinophilica. In the majority of his cases epididymectomy had been performed on the basis of the mistaken diagnosis. Considering the

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transitory character of the general condition a careful blood analysis should precede any surgical procedure

N Neoplastic Disease of Testis, Epididymis and Spermatic Cord

Neoplasms of the Spermatic Cord and of the Sheaths of the Testes

Introduction

Every enlargement of the scrotal contents of doubtful origin demands consideration of a possible neoplasm. Testicular tumors are preponderantly malignant and metastasize early Primary tumors are by no means exceptional and develop chiefly during the late twenties Seminomas however usually occur in men between thirty and forty years of age. Malignant tumors of the testicles in infants are always derived from congenital anomalies (cryptorchism) The imperfectly descended testicle is particularly exposed to injury and is very liable to undergo malignant transformation In rare instances primary cancer of the testis is bilateral the tumors appearing either simultaneously or several years apart. Primary neoplasms of the epididymis are uncommon and show a marked tendency to rapid progression. Secondary involvement of the testis and epididymis in malignant growth is due to cancerous invasion from adjacent tumors (carcinoma prostatae) or to metatastic deposits of cancer cells from distant tumors.

In this study we will not enter the discussion on the classification of testicular tumors. Up to the present time the interpretation and grouping of tumors of the testes have been subject to changes. Recent attempts to establish new classifications have been widely approved (Friedman and Moore 1946 Moon and Hullinghorst, 1948) but none has been hitherto accepted by all surgeons and pathologists The majority of all clinicians seem still to follow Ewing s definition of testicular tumors given in his work on *Neoplastic Diseases* (Philadelphia Saunders, 1940)

Ewing defined the overwhelming majority of testicular neoplasms as teratomatous tumors with little histological differences between seminomas and embryonal carcinomas *Thus the teratoid tumors include all neoplasms* designated as seminomas teratomas adenocarcinomas embryonal carcinomas, and chorio-epitheliomas, the latter forms developing from the embryonic chorion plate The teratoma pattern includes variations from primitive epithelial or mesenchymal to adult structures The so-called interstitial tumors, the rarest type are usually benign in character but occasionally undergo malignant degeneration

Cancer of the testicles may produce changes in the output of prolan A. Quantitative determinations however proved to be of less diagnostic value than expected. In a review of twenty six cases of cancer of the testis, Scully and Parham noted clinical evidence of hormonal imbalance

in nine patients six of the latter being children with precocious development. Three of the twenty adult patients showed gynecomastia. In four instances, orchiectomy was followed by partial or complete regression of these secondary symptoms Kimbrough and Denslow in a study on thirty two cases of tumors of the testis, stated that the results of the hormone test were often confusing and even caused delay in beginning of the treatment.

Symptoms

The first signs of malignancy may be inconspicuous. The initial painless hard, smooth or uneven, freely movable mass may escape the patient's attention for a considerable time As the neoplasm increases in size, however radiating pains develop as soon as the malignant process has reached the nerves of the tunica albuginea or epididymis Subsequently hydrocele may render any distinct palpation of the scrotal contents impossible.

Differential diagnosis: Early recognition of a malignant neoplasm of the testis depends first of all on the patient's early awareness of a mass in the testis and his prompt reaction in consulting a physician. The physician should regard any testicular enlargement of unclear origin as a danger signal which necessitates a careful examination including abdominal and rectal palpation and a careful search for a possible involvement of the regional lymph glands and retroperitoneal glands Many tumors of the testes metatasize very early

The *differential diagnosis* includes essentially syphilis tuberculosis and chronic inflammatory indurations of the testicle and epididymis. Even in the absence of serologic results indicating syphiloma, the possibility of a syphilitic orchitis must be considered. In syphiloma of the testicle however following an insidious onset, the tumor increases in size until some climax has been reached and then remains unchanged as a painless, circumscribed induration. Advancing cancer on the other hand, soon causes excruciating pains, which usually persist in any position of the body

Differentiation from tuberculosis is not too difficult, considering the onset of tuberculosis in the epididymis and its tendency to softening, suppuration and fistulization Testicular cancer seldom breaks through the tunica albuginea.

Little difficulties are encountered in the differentiation of malignancy from nonspecific or gonorrheal epididymitis, which begin as acute or subacute conditions, usually associated with fever and pains. Their limited duration and the gradual regression of the swelling will soon remove any doubt concerning their origin Residual infiltrations usually show a tendency to decrease in size

The limited value of the determination of the gonadotropic output into the urine has been mentioned.

In all doubtful cases *biopsy* will be most helpful to clear the diagnosis. For this purpose orchiectomy may be necessary regardless of the risk of occasionally removing a testis with a benign neoplasm. Surgeons, however, strongly advise that if malignancy is demonstrated, the biopsy should be followed immediately by radical removal of the lesion and of the regional and, if necessary, the retroperitoneal lymph glands. Such exploratory orchiectomy is indicated, for instance, when the presence of a concomitant hydrocele hampers a careful palpation. Aspiration of the contents of such hydrocele would implicate the risk to carry cancer cells from the affected testis into the tissues of the scrotal wall.

Neoplasms of the Spermatic Cord

The rare *primary* tumors of the cord are predominantly benign (lipomas, angiomas, leiomyomas) and only occasionally malignant (fibrosarcomas, cystosarcomas). D. Kershner described three separate tumors of the vas deferens in the same patient, a man of sixty-one years, and of these tumors two were lipomas and the third an angiomyxoma. Usually the neoplasms of the cord are located within the tunica vaginalis communis and may increase in volume to the size of an egg.

Neoplasms of the Sheaths of the Testes

Primary neoplasms of the sheaths of the testes, rare though they are, are of diagnostic importance. Either they envelop the scrotal contents without any adhesion to the scrotal wall, or in exceptional cases may be closely adherent to the scrotal wall. The latter type may be benign or malignant, and, as a rule, these forms are derived from congenital anomalies.

Recently Waller and Helwig gave a survey of the literature on "Cancer of the Tunica vaginalis" (1953) in connection with an observation of a primary tumor in a thirty-six-year-old man. This tumor could be differentiated and defined as a "dysontogenetic teratoid tumor" clinically and histologically resembling the embryonal carcinomas as found in the testis.

Fischer and Wolters described a diffuse tumor the size of a man's head, involving the sheaths of the testes. Following an injury the tumor underwent rapid malignant transformation. Postmortem examination revealed a polymorphous spindle cell sarcoma with many giant cells. The early recognition of the character of such tumor and its differentiation from chronic inflammatory thickenings may be difficult, especially in the

presence of chronic hydrocele with callous thickening of the scrotal wall, which does not transmit light and renders palpation difficult.

Therapy: The treatment of malignant neoplasms of the testes, epididymis and spermatic cord lies wholly within the field of surgery and roentgenotherapy Seminoma has proved to be the most radiosensitive neoplasm of the testis. L. G Lewis and other expert authors believe that the majority of seminomas if treated in time, will be cured by deep roentgenotherapy alone. Embryonal carcinomas do not respond satisfactorily to Roentgen rays. Chorioepithelioma is resistant to Roentgen treatment.

Radical surgery is still the therapy of choice in the majority of malignant conditions of the testes. Without entering upon any discussion upon surgical methods, it may be stressed that even following an early radical operation, the period of survival is usually limited to about one and one-half to three years. Especially in teratoid carcinomas and in seminomas in young individuals, the prognosis following surgical removal is poor Roentgenotherapy combined with, or following operation may prolong the survival period up to four or five years in some cases Roentgen treatment alone in inoperable advanced cancer of the testis may arrest growth of the tumor for a certain time and may mitigate pain and delay the general spread.

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CHAPTER 20

NONVENEREAL DISEASES OF THE CORPORA CAVERNOSA

A. Introduction
B. Traumatic Cavernositis
C. Non-gonococcal Bacterial Cavernositis
D. Tuberculosis of the Corpora Cavernosa
E. Malignant Neoplasms of the Corpora Cavernosa
F. Priapism
G. Induratio Penis Plastica
References

A. Introduction

Inflammatory affections of the corpora cavernosa are not uncommon, but the non-gonorrheal types are rare. Trauma, bacterial infection derived from the urethra or periurethral phlegmon, tuberculosis or tropical diseases may involve the cavernous bodies. Metastatic bacillary cavernositis has been reported in association with typhoid, typhus, smallpox or septicemia. In such cases abscess formation is not uncommon and gangrene of the penis may result.

Of particular importance, is the involvement of the corpora cavernosa in cases of malignant growth and in diseases of the hematopoietic system. This aspect will be discussed in the section on priapism.

In addition, attention must be directed to a variety of chronic indurative processes of the penile tissues, in particular to the plastic induration (induratio penis plastica) a fibrosis of the cavernous bodies which appears to be related to other fibrotic conditions of the mesenchymal tissues.

B. Traumatic Cavernositis

Ruptures of the corpora cavernosa due to blows, kicks or crush injuries, are usually limited to the tunica albuginea. Deeper lesions such as lacerations caused by explosive missiles may however involve all the tissues of the penis including the urethra. Hematoma and swelling the foremost symptoms of subcutaneous rupture, are frequently followed by thrombosis

of the cavernous spaces and of the efferent blood vessels Rupture of the urethra opens the way to secondary infection of the urinary tract.

Christeller and Jacobi reported fatal periurethral phlegmon due to a brusque introduction of graduated sounds into a resilient stricture in a man of twenty-one years Autopsy revealed a septic infiltration of the cavernous bodies and prostate, with abscess formation and thrombophlebitis of the pelvic veins Forcible rupture of the cavernous bodies has been described in the literature as the result of fracture or torsion of the erected penis (fractura penis) due to sexual excess. The *treatment* of subcutaneous rupture is chiefly conservative. The natural process of healing should not be interrupted by manipulations which might produce further lesions of functionally important tissues

C. Non-gonococcal Bacterial Cavernositis

The clinical symptoms do not differ from those of gonococcal cavernositis. An *inflammatory infiltration* followed by softening and fre-



FIGURE 140 Cavernositis, abscess formation. (Wildbolz, H *Textbook of Urology* Berlin, Springer 1924)

quently by abscess develops in the middle third of the pars pendula, exceptionally in the perineoscrotal region. Tenderness to touch painful erections and micturition associated with fever are more or less conspicuous symptoms. Aspiration will yield smears and cultures showing pathogenic

bacteria. Various bacilli have been demonstrated in non-gonococcal cavernositis. Fiser described purulent cavernositis due to *B. coli* infection of the urinary tract, Sewell *et al.* cavernositis with abscess and fistula formation, showing pseudodiphtheria bacilli in the smears and cultures. Purulent cavernositis demands early surgical treatment if trials with aureomycin and other antibiotics proved futile.

D. Tuberculosis of the Corpora Cavernosa

Tuberculosis of the corpora cavernosa is a rare complication of urogenital tuberculosis leading to formation of fistulae and sinuses. It is only in exceptional cases of tuberculous cavernositis that the urethral wall is not affected (Buzzi). In such a case, the aspirated pus taken from an egg-sized perineal swelling contained tubercle bacilli and this finding provided the clue for diagnosis of a previously undetected renal tuberculosis.

Bilharziasis of the penile tissues frequently involves the cavernous mesh work, granulomatous and fibrotic changes cause deviations of the erected penis or result in impotentia coendi.

E. Malignant Neoplasms

Malignant neoplasms may invade the cavernous bodies from neighboring tumor masses, or may occasionally be of metastatic origin. *Primary* neoplasms of the cavernous bodies are rarities. However, unquestionable cases have been described as, for instance, by Vintici and Alterescu (round cell carcinoma) and Yamamoto (hemangioendothelioma). Secondary involvement is less uncommon and has been reported in primary carcinomas of the urethra, carcinoma of the bladder or prostate, or due to metastatic hypernephroma (Craig). This list does not, of course, exhaust the variety of tumors that may be encountered. Generally carcinoma prevails; sarcoma of the corpora cavernosa is extraordinarily rare.

The *clinical manifestations* of tumors of the cavernous tissue correspond to the site, extent and consistency of the respective neoplasms. Frequently a striking deviation of the penis during erection first attracts the patient's attention. This diagnostically important symptom will be discussed in the section on priapism.

The *differential diagnosis* includes (1) plastic induration of the corpora cavernosa, (2) tuberculosis, and (3) syphiloma of the cavernous bodies. Tuberculous cavernositis tends toward softening, fistula formation and ulceration. Other symptoms of urogenital tuberculosis will support the diagnosis. On the other hand, malignant growth produces a nodular or diffuse induration with a marked tendency to progression and subsequent involvement of the regional lymph glands. The rare syphiloma of the cav-

ernous bodies is almost always unilateral and circumscribed forming a nodular or cylindrical induration. Other manifestations of syphilis may aid in diagnosis, although a positive serologic test will not definitely exclude a coincidental tumor development. The differentiation from plastic induration of the penis will be discussed in connection with the latter condition.

The *therapy* of malignant neoplasms of the cavernous bodies lies in the domain of the surgeon and roentgenologist. The treatment of nongonococcal bacterial cavernositis consists in early opening of the abscesses. Usually the administration of antibiotics should precede the surgical procedure

F Priapism

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Introduction

No other condition of the corpora cavernosa, so convincingly demonstrates the need for a careful general examination in nonvenereal affections, as does the phenomenon of *priapism* with its multifarious etiology and the diagnostic problems involved. Various etiological classifications have been presented.

Priapism is the term to designate a permanent excessive erection of the penis, which differs from the physiological erection by its painfulness the lack of sexual desire and the persisting ability of the patient to void *urine during the state of erection. As a rule, this type of erection is not as*sociated with ejaculation. Efforts of the patient to release himself by sexual intercourse always result in failure Spells of excessive erections may precede the onset of priapism.

Frequently the condition comes on suddenly without any premonitory spells and may surprise the patient during his night's sleep or following intercourse or micturition. The duration of priapism varies considerably from several days or weeks to months and, in exceptional cases even up to a year In the majority of cases, medical aid will be required, although in some cases the condition subsides spontaneously with or without resulting functional damage.

True priapism involves only the corpora cavernosa penis. The corpora cavernosa urethrae as well as the spongy tissue of the glans which com

municates with the cutaneous penile veins are very seldom involved. Therefore the patients are capable of voiding urine during the state of erection.

As Fulton explains, normal erection results from an increased flow of blood into, and a restricted venous return from the corpora cavernosa, the principal factor being the arterial dilatation. The restriction of venous return is largely passive. Arterial dilatation is induced by stimulation of the pelvic splanchnic system (nervi erigentes) whereas vasoconstriction and subsidence of the erection depend upon a stimulation of the sympathetic nervous system. Every disturbance interfering with this mechanism results in dysfunction. Increased afflux of arterial blood may be caused by irritation or lesions of certain parts of the central and peripheral nervous system. Restriction of the venous afflux usually results from obstruction of the cavernous spaces in connection with hematoma, thrombosis, abscess, or malignant growth.

Traumatic Priapism

Trauma of the cavernous bodies produces swelling, hematoma and thrombosis. A state of priapism may thus result and will not subside until the obstructing blood masses have been surgically removed. Even a seemingly slight trauma may be followed by priapism. Erections of long duration may also occur as a result of incarcerated intraurethral concrements. Also indirect trauma, such as a fall injuring the peritoneum or a concussion of the pelvis may be followed by priapism.

Priapism Due to Urethral Irritation or Inflammation

Frequent and prolonged erections occur after sexual excess or habitual masturbation. They are common in acute gonorrhea, especially in gonorrhea of the posterior urethra. This clinical symptom is easily controlled by administration of sedatives or introduction of belladonna suppositories.

Occasionally priapism may be caused by *intra urethral papillomas* thus confronting the physician with a diagnostic problem. Annoying nocturnal erections of ten to twenty minutes duration, associated with a burning sensation on micturition or a slight discharge, may lead the patient to consult a physician. The urine is clear or hazy with or without an admixture of blood. There may be a few epithelial cells and some leukocytes without bacteria. The discharge may disappear temporarily. Urethroscopy reveals the presence of papillomas, frequently located near the colliculus seminalis. Symptoms disappear promptly following surgical removal of the warts.

Thrombophlebitis plays an important role in the pathogenesis of priapism. Even in the earlier literature, we find reports on priapism in connection with paraurethritis gonorrhoica due to thrombophlebitis of the vena profunda penis or due to a septic infection of the pelvic veins, as observed in complicated appendicitis (Rosenthal). Drè Kolias described priapism associated with appendicitis in a man of thirty nine years. Increased erections preceded the onset of priapism. At operation the appendix was found dislocated into the lower part of the pelvic cavity and in close contact with the vesiculae seminales. Erection subsided promptly following the operation.

Priapism as a Syndrome of General Infectious Diseases

Priapism as a syndrome of general infectious diseases has also been described by earlier writers but recent reports are scarce. Imbert observed priapism in a case of rheumatic fever, its onset coinciding with that of the fever. A similar case was reported by Patel in which the erection persisted for twenty-one days coincident with febrile relapse. Chalier described an erection lasting fourteen days occurring in convalescence from typhoid (post typhoid phlebitis). Further clinical investigation of this subject is needed.

Malignant *Priapism*

Malignant priapism is the term applied to all cases associated with malignancy of the corpora cavernosa. The etiology and pathology have been discussed in the preceding section. The erections resulting from tumor infiltration differ from true priapism, the resulting deviation varying with the site and extent of obstruction of the cavernous spaces. A state of semi erection prevails in malignant cases and may persist after death.

Priapism Persisting after Death

Priapism persisting after death attracted the attention of pathologists of all times. It has been observed following malignant priapism, leukemia or thrombophlebitic obstruction. As early as 1861 the pathologist Rokitansky described priapism still existing after death in a case of myelogenous leukemia in which the erection developed six weeks before death. Priapism persisting after death was also demonstrated by Nauwerk and Delbanco and has been discussed in Jadassohn's *Handbuch der Haut-und Geschlechts krankheiten*, Vol. XXI. Priapism developed eight days before death in a youth of nineteen years who died of septic polyarthritis and endocarditis. Autopsy revealed an extensive thrombosis of the vena pudenda inferior and the plexus prostaticus.



FIGURE 141 Case of N wark and Delbanco post mortem examination, state of priapism at autopsy (F Callomon Priapismus. *Handbk. Haut-und Geschlechtskr* XXI p 209 J Springer Berlin, 1927)

Scheidegger reported thrombophlebitis of the pelvic and abdominal veins extending into the penile veins in two instances of priapism continuing to exist after death. In both cases, the obstruction was limited to the corpus cavernosum urethrae which is otherwise never involved in priapism. In a third case, the same author found both the corpora cavernosa penis and urethrae filled with blood masses

Priapism—A Manifestation of Blood Diseases

Priapism occurs in acute or chronic leukemia and other diseases of the hematopoietic system It has been observed as an *initial* symptom in myelogenous leukemia, and its presence has occasionally been the indication for the first blood analysis, thus proving its diagnostic importance (Achard, Macciotta, Conn, *et al*) Spells of excessive erections may precede priapism in these cases The leukemia observed in such cases has been predominantly of the splenomyelogenous type *Pathologic anatomical* findings In Rokitansky s case the cavernous spaces were filled with pale

reddish pulpy masses intermingled with pus derived from the abscesses that had formed around the prostatic part of the urethra. Recently Warthin observed thrombotic masses obliterating the cavernous meshwork as well as the vena dorsalis penis.

In 1895 A. Kast contributed his classic study on the pathologic changes caused by leukemia in the cavernous tissues. In the autopsy material taken from a case of leukemic priapism a cross section of the penis showed the corpus cavernosum urethrae unchanged the structure of the corpora cavernosa penis however was hardly recognizable. Microscopically the cavernous spaces were enclosed in a dense connective layer filled with polymorphonuclear cells and lymphocytes. Except for a few slit like spaces, the central areas of the cavernous meshes consisted of a homogenous con nective tissue, a metaplastic end product of leukemic thrombosis

Priapism in Sickle-Cell Anemia

Priapism in *sickle-cell* anemia was first studied by Diggs and Ching Kemp and Hosey collected fifteen cases covering the period from 1934 to 1950 Preceding transitory erections have been repeatedly reported. Campbell observed priapism as an initial symptom of sickle-cell anemia. Accord ing to Diggs and Ching, this form of priapism is caused by a mechanical interlocking of the elongated and spiked blood cells which are hindered in their transition through narrowed spaces Gotzoff believes that the chief factor consists of a "lowering of the oxygen tension and a temporary reduction of the pH of the blood and subsequently of the release of those hematologic factors which influence sickling Due to stasis, an unusual cohesive attraction and a tendency to rouleaux formation may lead to thrombosis.

Priapism Due to Chemical Intoxication

Recent studies have been devoted to the role of the *hyperviscosity of the blood* in the pathogenesis of permanent erections Rotenberg explained that blood viscosity depends on (1) the blood content of corpuscular elements (2) the volume of these elements (3) the hemoglobin content (4) the amount of albuminous substances and salts, and (5) the carbon dioxide content of the blood. An abnormal increase of solid carbon dioxide in the blood is always associated with increased viscosity Even in ancient literature we find references to priapism associated with *carbon dioxide intoxication* In 1747 priapism is described as occurring in workers who had been exposed to carbon dioxide fumes while employed in cleaning an old well. The phenomenon of priapism in persons dying from suffoca tion hanging or strangulation (accumulation of solid carbon dioxide lead

ing to irritation of the bulbar vasodilator center) is likewise well known. Landois and also Nikolsky succeeded in producing priapism in animals by injecting blood from suffocated animals or muscarin.

Priapism due to *chemical intoxication* has been reported in cases of acute or chronic lead intoxication, as for instance, in workers in printing plants or chemical factories. Following transitory erections priapism may develop. In all such cases, recovery was prompt following withdrawal from work.

Overdoses of *aphrodisiacs* or of hormonal substances occasionally produce priapism. Such instances have been observed following abuse of cantharidine, yohimbin, or androgen therapy. Finkler reported priapism in an eunuchoid after the first of several injections of testosterone propionate. The erection lasted for seventeen days, but did not recur during a later second series of injections.

Lipton and Toomey (1952) described priapism following an injection of 1,500 units of *tetanus antitoxin*. An earlier injection given to the same patient eleven years before, was followed by hives. A skin test preceding the present administration proved negative. However, two days after injection, the sight of injection was reddened and subsequently a painful erection developed which still persisted on the seventh day after administration when patient was hospitalized. Not before aspiration of the obstructing blood masses did the priapism recede gradually. The patient had never had gonorrhea or other urogenital disease.

The possible relation of priapism to *diseases of metabolism* remains a problem for clinical investigation. Reports in recent literature are scarce and inconclusive. Earlier writers described priapism in connection with gout or diabetes (literature up to 1911 collected by Scheuer). Hinman, in checking the literature some years later, found only four indisputable cases of priapism associated with gout.

Idiopathic Priapism

Idiopathic priapism is the term still reserved for cases of obscure origin. In the majority of such cases, the only pathologic finding has been dark, syrupy homogenous blood masses in the distended cavernous spaces, with no coagula. Recent research has yielded new aspects to understand the pathogenesis in cases of idiopathic priapism.

A patient of twenty-two years, whose case was reported by Chauvin, was embarrassed on his wedding trip by a painful persisting erection. After suffering for four weeks, the blood masses were removed. Hyperviscosity of the blood had impaired the capillary circulation in the penile venous system. The author suggested that many obscure cases of prolonged erections may be due to capillary stasis rather than to thrombosis.

As a matter of fact, hyperviscosity of the blood is well known in leukemia and polycythemia (Rotenberg, 1935) Opinions differ as to whether the hyperviscosity of the blood found in the contents of the cavernous bodies in priapism is always associated with hyperviscosity of the circulating blood. Cuccioli demonstrated such a coincidence in blood specimens taken from both the corpora cavernosa and from an arm vein of the same patient On the other hand, Cassuto in a series of personal observations was never able to demonstrate any such concurrence This aspect demands further investigation.

Priapism Due to Diseases of the Nervous System

Priapism due to diseases of the nervous system has been observed in most dissimilar affections. Thus we find reports of its incidence in association with injury of the lumbar spinal cord or the brain with encephalitis, meningomyelitis, vertebral tuberculosis or neoplasms compressing the spinal cord tabes dorsalis epilepsy hysteria or mental disease. Most significant is the incidence of increased erections as a premonitory symptom of *tabes* The French syphilologist, Fournier was the first to emphasize the diagnostic importance of this initial symptom The erections in early tabes are characterized by lack of sexual desire and, at the same time by diminished sexual potency The erections rarely endure for more than several hours. Fournier described the case of a tabetic physician who suffered from priapism during the entire second half of the night.

Differential diagnosis: Frequently the patient's history and a careful general examination will yield the clue for an etiological diagnosis As a rule a complete blood analysis is indicated Neoplastic involvement of the cavernous bodies has been previously discussed on page 333 In an obscure case of priapism, Alcock was able to make an early diagnosis of malignancy from material aspirated from the distended and indurated cavernous bodies The microscopic examination revealed cancer Septic thrombophlebitis may be suspected as a cause of priapism, when the patient presents general symptoms of septic infection

Therapy: Each case of priapism requires individual treatment according to its cause Control of the basic disease is of foremost importance.

In sickle-cell anemia, it is necessary to resort to surgical procedures to remove the obstructing masses of blood.

In leukemic priapism Roentgen therapy is the treatment of choice. The leukemic cell masses filling the cavernous spaces are radio-sensitive and readily respond to treatment. Recurrences however occur according to the general state of the leukemia. Therefore treatment of the disease itself should also be carried out

Persisting erections due to cancerous obstruction of the cavernous

spaces may respond temporarily to Roentgen irradiation, but radical surgical measures are necessary in most instances

Aspiration of the hemorrhagic contents after puncture or incision of the involved cavernous bodies has proven satisfactory in cases of priapism due to stasis or thrombus formation in pelvic veins or in idiopathic priapism. This may then be followed by saline irrigation of the emptied blood spaces. Great caution is necessary however to avoid additional damage to intact cavernous tissue when removing large areas of blood after incision.

In excessive prolonged erections occurring after sexual excess, inflammatory conditions of the posterior urethra or in psychogenic problems, the administration of sedatives, narcotics, or hypnotics may be helpful in eliminating the condition. Such palliative therapy may be helpful in priapism associated with spinal cord lesions The rare cases of syphilitic priapism have responded to specific therapy whether the syphilitic lesion has been a local syphiloma or is a result of central nervous system syphilis.

G Plastic Induration of the Corpora Cavernosa Penis (*Induratio Penis Plastica*)

Definition and Nomenclature

Induratio penis plastica is characterized by (1) circumscribed solid indurations derived from the sheaths of the cavernous bodies (2) the lack of inflammatory symptoms (3) a slow insidious beginning followed by a chronic course, and (4) pronounced resistance to treatment.

Earlier nomenclature such as ganglion penis (Ricord, 1847) noeuds des corps caverneux (Nélaton 1859) plaque indurée (Tuffier 1885) and cavernitis senilis (Horowitz, 1900) has disappeared from the literature The name Peyronie's disease has survived, however although not many physicians may know that François de Peyronie was the court surgeon of Louis XV and the founder of the Academie Royale de Chirurgie. He was the first to contribute an accurate clinical description of the condition in 1743 His name may justly be coupled with this condition, in the same manner that the closely related contracture of the palmar fascia is coupled with the name of Dupuytren, who first described that condition in 1832.

In the American literature, the disease was known as "Van Buren's Disease following this author's description published in 1874. Even today there still exists some confusion in terminology The name fibrous cavernositis used by recent authors is certainly a misnomer considering the non-inflammatory character of the condition. And even more confusion has been added by foreign authors applying the term plastic induration as a collective name for most dissimilar fibromatous affections of the cavernous

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Persisting erections due to cancerous obstruction of the cavernous

palpable also during erection As a rule, the corpus cavernosum urethrae is not involved.

The onset of the disease is slow The indurations are painless in the initial stage later on pains develop during erection. The course is extremely chronic and frequently extends over many years, with a very low tendency to spontaneous regression. Beginning at some point of the shaft the induration may remain limited to a solitary plaque or nodule. After



FIGURE 143 Sketch of indurations palpable from the lateral aspect of the penis. Large cord-like induration superimposed upon a deeper nodule of the tunica albuginea. (61 year old man.)

a period of slow progress the morbid process usually reaches a climax, followed by a temporary or permanent standstill.

In several instances, spontaneous regression has been convincingly demonstrated. One of our patients, a man of fifty three years, when examined two years after the first consultation, showed merely a tiny residue of a previously hard, annular induration near the sulcus coronarius, and even this remainder disappeared later after a total course of four to five years. There had been no treatment whatsoever The patient had sought medical advice because he feared cancer Other irrefutable instances of



FIGURE 144. The same patient. Dorsal aspect.

spontaneous regression either partial or total, have been cited by O Sachs and other authors. Rare though they are these observations should not be overlooked.

As mentioned above many patients become aware of the disease only when *deviation of the penis in erection* interferes with the sexual act. Incurvation upon erection is the very first alarming symptom. The type and degree of the incurvation will vary with the site and extent of the fibrotic process. The deviation develops gradually after months or even

years. Pains may be present or may be lacking even in cases with multiple indurations On the other hand, a single rigid nodule may suffice to produce radiating pains during erection Deviations are directed either toward one side (strabismus penis) or may be arched with an upward concavity Exceptionally bayonet like deviations have been described. Difficulties in marital relations ensue, especially when impotentia coeundi develops as an end effect. It is no wonder that the majority of these patients develop sexual neurasthenia. When treatment fails many a patient will

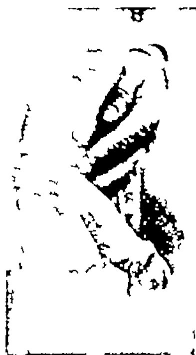


FIGURE 145 Penis in semi-erection showing incurvation. (Sonntag, E. *Arch Clin. Chir* 117 612, 19_1 Fig. _)

sink into a state of despair Mental repercussions with a suicidal trend have been described

Induratio penis plastica, long unknown to the practitioner began to attract general attention when the coincidence of this condition with *Dupuytren s palmar contracture* in one and the same patient had been repeatedly encountered. Soon the question arose as to whether this coincidence signified anything more than a casual association. Although such a combination occurred much less frequently than either of the mentioned conditions alone the number of case reports increased giving rise to comparative studies

Occasionally also other fibromatous affections have been observed in association with induratio penis plastica and Dupuytren s disease in particular keloids. The incidence of induratio penis plastica combined with

Dupuytren's disease has been estimated as about 10 per cent of all cases of the penile condition (Zur Verth and Scheele, E. Sonntag Heite and Siebrecht) Every surgeon urologist and pathologist when confronted with the one affection should look for the possible coexistence of the other

Pathology and Histology

Every description of surgical specimens of removed indurations emphasizes the hard consistency and whitish or bluish white aspect of the extirpated masses, resembling keloid tissue As a rule, no difficulty is experienced in separating the indurations from the underlying tissue. Sometimes, however the indurations were found adherent to the cavernous tissue or



FIGURE 146 Roentgen picture of the penis of (a) Dachshund (b) Baboon and (c) Monkey (Cebus capucinus) (Jacoby M. *Ztschr urol. Chir* 16 105 19_4, Fig. 3.)

extended deeper into the septum penis It is generally agreed that the fibrotic process begins in the tunica albuginea.

Another characteristic of induratio penis plastica is the occasional finding of *calciferous cartilaginous or osseous particles* embedded in the fibrotic tissue. Their size and shape vary from tiny irregular particles to splinter like inclusions which are easily demonstrable in roentgenograms. They have been erroneously interpreted as atavistic remnants analogous to the os priapi" or os penis of animals described in monkeys, bears, weasels, cats, guinea pigs and marsupials. But there is no such phylogenetic throwback. The os penis of animals is a functionary important finely constructed organ connected with the septum penis, developing in harmony with natural growth processes. The human os penis, on the contrary is so to speak, a secondary metaplastic product. These products of meta

plastic ossification are always embedded in the sclerotic tissue of the tunica albuginea or the septum penis In addition, calcified particles may be found in the afflicted tissue (*Christeller Zur Verth and Scheele*)

It is a significant fact that similar calcification and ossification occur in the fibrotic tissue of Dupuytren s disease. Metaplastic ossification is like wise well known in other fibromatous lesions such as laparotomy scars scars from gunshot wounds and in myositis ossificans.

Histologically the structure of plastic indurations and of the diseased



FIGURE 147 Roentgenogram of ossified induration showing osseous inclusions in induration. (Zur Verth and Scheele *D Zetschr Chir* *121* 298, 1913 Figs. 1 and 2.)

palmar fascia shows a fibrous tissue poor in nuclei devoid of elastic fibers, and poor in blood vessels. Inflammatory changes are lacking in both diseases. Special attention has been directed to characteristic cell accumulations around the walls of the smallest blood vessels. They consist of oval or spindle-shaped cells with a finely granulated protoplasm and large nuclei. They encircle the capillaries in two or three concentric rows (fibroblasts O Sachs Bildungszellen, Rothschild) These findings have been confirmed by other investigators (Wiedhopf Delbanco Frangenheim) These cell accumulations have been generally defined as embryonic rests and are believed to form the starting point of the plastic indurations

In Dupuytren s disease analogous cell groups have not so far been

clearly described. However Janssen and also Krogius assumed that also in Dupuytren's contracture, the fibrosis proceeds from the walls of the small blood vessels. Horwitz, on the other hand, in recent elaborate studies, could find no evidence for any such assumption. Nevertheless all interpretations hint at the possible presence of pre-existing embryonic elements



FIGURE 148. Induratio penis plastica. Microscopical picture. Connective tissue of Albuginea transformed to an uncharacteristic tissue poor of nuclei and vessels; loss of elastic fibers. (Sonntag, E. *Arch. Clin. Chir.* *117* 614, 1921, Fig. 7.)

responsible for the fibromatous process in both induratio penis plastica and Dupuytren's disease.

The *etiology* of induratio penis plastica is still obscure. There is no connection with venereal diseases. The long disputed concept that gout, diabetes or arthritis play an essential role in the pathogenesis was based

on inadequate material Only one of our own thirty five patients had diabetes and none had gout or arthritis In a series of two hundred cases checked by Zur Verth and Scheele gout was recorded in thirteen diabetes in twelve and arthritis in fifteen cases Similarly Horwitz, in a series of



FIGURE 149 Section from an induration showing ossification and cartilagenous elements. (Sachs, O *Arch Dermat Syph* 55 53, 1921 Table 6 Fig 3.)

thirty five cases of Dupuytren's palmar disease found only one instance of gout and one instance of diabetes

The concept of earlier investigators who labeled plastic induration of the penis as a special disease of advanced age gave rise to objections,

since the occasional occurrence of the condition in very young individuals had been noted (see p 342) Occasionally also Dupuytren's contracture has been observed in young individuals (Janssen two youths of eighteen and nineteen years of age) Nevertheless time and again the question arose whether there may exist some relation between the involutionary process of advanced age and the development of plastic induration as observed in the majority of cases in men of forty to sixty years. The reader is referred to Heite and Siebrecht (1950) This problem remains open for further investigation.



FIGURE 150. Embryonal mesenchymal cells ("Fibroblasts") embedded in connective tissue poor of nuclei and vessels. (Sachs, O: Ibidem, Table 5, Fig. 1)

The trend of our time to bring clinically and histologically similar affections of unknown origin into a common denominator led to extended comparative studies of various diseases of the connective tissue At tempts have been made to form a new disease entity on the basis of an identical histological picture

Earlier comparative studies of renown pathologists such as von Gaza Frank, *et al.*, who described Dupuytren's disease, plastic induration of the penis, nasopharyngeal fibroids and keloids as etiologically related conditions have been resumed in more recent times. In addition, Horwitz (1942) included the desmoid of the abdominal wall, Heite and Siebrecht believed the fibrosis mammae virilis to be related to plastic induration of the penis. The authors ascribe all the above-mentioned affections to a

peculiar individual reaction of the connective tissue to various irritations. Endocrine disturbances or changes of the metabolism and malnutrition are thought to be the factors releasing fibrotic proliferation This hypothesis of a possible individual predisposition (*fibroplastic diathesis*) has been generally accepted

In recent times, momentous objections have been made against too far reaching conclusions based essentially upon similarities of the histological picture in diseases of the mesenchymal tissue. Not long ago (1953) O Gans emphasized that new research on the pathology of the connective tissue with new staining methods has shown that an obvious similarity of the histological pictures may not suffice to assume an identical pathogenesis and etiology of the respective conditions

However when comparing the fascial hypertrophy in plastic induration of the penis and that in Dupuytren's palmar disease, the assumption of a close relation between both affections is supported by the frequent coincidence of these two conditions in the same individual and in addition by clinical and histological similarities including hereditary factors.

Congenital disposition and heredity are known to play a part in Dupuytren's contracture keloids, and apparently also in plastic induration of the penis The reports of a familial incidence of palmar contracture are numerous. Krogius mentioned observation of palmar contracture in four brothers their father and grandfather Sprogis traced a familial incidence of Dupuytren's disease in seventeen members of related kin back to the year 1750 Berg recorded this disease in three sets of twins, all developing the disease at about the same age Couch reported palmar contracture involving the same fingers of the same hand in monozygotic (identical) twins. These reports certainly encourage investigation along these lines concerning induratio penis plastica.

Contrastingly analogous reports are very scarce in plastic induration of the penis. Bruhns (1925) reported the case of a man of fifty nine years, whose brother of sixty years suffered from the same condition. We found only two similar instances in recent literature Ungerer (plastic induration in father and son) and Vonessen (plastic induration in two brothers) It goes without saying that investigation of this aspect is difficult because patients tend to hide their genital condition as long as possible and are seldom capable or willing to admit similar conditions in their ancestry

The concept of the existence of a congenital disposition is corroborated by the previously mentioned findings of embryonal cell elements in the sheath of the corpora cavernosa. In response to various disturbances such as endocrine dysfunction, these embryonal residues may become the starting points of the fibrotic process.

The possible role of *trauma* in the pathogenesis of plastic induration is still under discussion Regarding Dupuytren s palmar disease it is not gross injury by accident that has been considered to cause the fascial disease, but the continual sequence of slight trauma. However the old theory that the palmar disease is a disease of manual workers exposed to occupational traumatization had to be abandoned, since not infrequently the condition had been observed also in intellectual workers, such as scientists, artists and priests. Bunnel, in his *Surgery of the Hand* bluntly states that Dupuytren s disease is unrelated to trauma.

Regarding the penile disease traumatization from sexual intercourse can hardly play an essential role since otherwise the condition would probably be more common considering the general exposure of all men. There remains only the question, as to whether trauma may act occasionally as a trigger mechanism by provoking proliferation of the connective tissue in predisposed subjects Such an assumption will not withstand critical consideration. In no case has it been possible to deter mine definitely the time of the onset of the indurative process. The first changes may have been present long before such an accident.

Differential Diagnosis

Diagnostic difficulties are encountered particularly in the initial stages and especially in the presence of a single nodular induration. Distinction from residual lesions of gonococcal para or periurethritis is fairly easy Post-gonorrheal infiltrations involve the urethral wall and may be found in any part of the urethra. Plastic indurations never involve the urethral wall, but are superimposed on the cavernous bodies, and are as a rule, palpable from the dorsal surface of the penis.

Lymphogranuloma venereum may produce infiltrations of the penile tissue which, in the late stages of development, may leave nodular or cord like indurations simulating induratio penis plastica. In such cases, a positive Frei reaction may reveal their origin. A positive Frei test is never caused by genuine induratio penis plastica. However induratio penis plastica may occur incidentally in a patient previously stricken by lymphogranu loma venereum In countries where lymphogranuloma venereum is seen more frequently the term plastic induration is generally employed to designate the classic form of induratio penis plastica as well as certain sclerotic products of lymphogranuloma venereum Thus, case reports on plastic induration of the penis are more numerous in Spanish Latin American and Mediterranean countries.

The rare syphiloma of the corpus cavernosum is unilateral and usually not palpable during erection like the plastic indurations.

Primary or metastatic neoplasms of the cavernous bodies not infre-

quently simulate plastic indurations. Initial cancer of the bodies may appear as a circumscribed painless hard nodule under a freely movable skin. An observation of Kreibig illustrates the possible differential diagnostic difficulties his patient showed a solid plate the size of a shilling palpable under the skin. Biopsy revealed a purely fibroid structure and suggested induratio penis plastica. After eight months another induration developed and its location on the inferior aspect of the penis seemed to contraindicate plastic induration Radical surgery and histologic examination revealed a myosarcoma of the penis

Therapy

Not so long ago resistance to treatment of any kind seemed almost pathognomonic of induratio penis plastica. Surgery appeared to offer a chance for radical cure in only a limited number of cases. A rigid selection of cases to be referred for surgical treatment is imperative to prevent relapses. Radical extirpation is always difficult in the presence of multiple indurations dispersed all over the corpora cavernosa or in cases where proliferations extend into the septum penis. Recently Lowsly and Boyer (1950) stressed that surgery will yield most promising results if performed in the *early* stages of induratio plastica.

A marked improvement in therapeutic results followed the advent of radium as a method of treatment. In addition prospects of cure were enhanced by advanced technics in Roentgen therapy Today the application of *radium is the treatment of choice* At least half of the patients treated may receive definite benefit (Fricke and Varney Mayo Clinic, 1948 evident regression or definite cure in about 55 per cent of one hundred and forty-one cases of plastic induration of the penis receiving radium treatment)

Success of radiotherapy depends to a large extent on the structure of the fibromatous tissue Indurations consisting of young fibrous texture apparently offer the best chances for a complete cure by radium therapy Results are not so satisfactory in the presence of irreversible cartilaginous or osseous enclosures which will be responsible for nodular residua. There would be little sense in attempting to ensure healing by indefinite prolongation of radium treatment. A series of at most six to eight seances at proper intervals and with correct dosage has been suggested for cases that respond slowly However already after the first two or three applications, a softening of the indurations has been noted in the majority of cases.

If radium is not available *roentgenotherapy* should be tried. Results, comparable with those obtained with radium therapy will depend largely upon the technical experiences of the roentgenologist In spite of recent advances in the selection of the proper quality of irradiation and the proper

dosage for Roentgen therapy incomplete cures seem to be still more common after Roentgen than after radium treatment. Molineaus (1951) however obtained equal results after radium and Roentgen irradiations in extended comparative studies.

Recently C. L. Steinberg reported beneficial effects obtained by the administration of *tocopherols (Vitamin E)* in *Dupuytren's contracture* with a dosage of 300 mg. administered orally in divided doses of 100 mg. three times daily Following Steinberg's procedure, Thomson noted evident benefit in five of ten cases of palmar contracture. Scott and Scardino employed a compound of mixed tocopherols natural type ("Eprolin" Lilly & Co.) in twenty-three patients with *induratio penis plastica* Softening and regression were marked in six cases, moderate in fifteen cases, and in two the condition remained unchanged Additional beneficial results have been reported by Steinberg (1951) R. A. King, on the other hand, used vitamin E in the treatment of *Dupuytren's contracture* but was unable to observe any beneficial effect in twelve of thirteen patients. Further trials will be needed to determine the possible usefulness of tocopherols in the treatment of these two conditions.

In attempting to evaluate the results of any medical treatment administered over a period of months it must be kept in mind that spontaneous disappearance of indurations even though rare, has been repeatedly demonstrated.

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